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(54) Title: NOVEL FAMILY OF PHEROMONE RECER	TORS			

(57) Abstract

The invention describes a multigene family encoding a collection of novel mammalian pheromone receptors. Nucleic acids encoding the pheromone receptor polypeptides, including fragments and biologically functional variants thereof are provided. Also included are polypeptides and fragments thereof encoded by such nucleic acids, and antibodies relating thereto. Methods and products for using such nucleic acids and polypeptides also are provided.

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NOVEL FAMILY OF PHEROMONE RECEPTORS

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Field of the Invention

This invention relates to nucleic acids and encoded polypeptides which are part of a multigene family encoding a collection of novel mammalian pheromone receptors. invention further provides representative nucleic acids and encoded polypeptides in this multigene family. The representative polypeptides are expressed in the murine and rat vomeronasal organ (VNO). Agents which bind the nucleic acids or polypeptides also are provided. The invention further relates to methods of using such nucleic acids and polypeptides in the diagnosis and/or treatment of disease, including the use of these molecules in controlling fertility and behavior in vertebrates and invertebrates.

Background of the Invention

Pheromones are intraspecific chemical signals found throughout the animal kingdom. They regulate populations of animals by inducing innate behaviors and stereotyped changes in physiology (Karlson and Luscher, Nature, 1959, 183:55-56; Wilson, Sci. Am., 1963, 208:100-114; Sorensen, Chem. Sens., 1996, 21:245-256). Pheromones can serve as cues for overcrowding, impending danger, reproductive status, gender, or dominance. In rodents, a variety of pheromone effects have been reported. These include effects on estrus and the onset of puberty as well as the induction of mating and aggressive behaviors (Singer, A.G., J. Steroid. Biochem. Molec. Biol., 1991, 39:627-632; Halpern, M., Ann. Rev. Neurosci., 1987 10:325-362; Wysocki, C.J., et al., In the Neurobiology of Taste and Smell, 1987, 125-150; Novotny et al., Chemical signals in Vertebrates, 1990, Vol. 5, eds. D.W. Macdonald et al., Oxford University Press).

The detection of pheromones is mediated by the olfactory system. However, sensory neurons that detect pheromones are typically segregated from those that detect volatile odorants (Keverne, E.B., Trends Neurosci., 1983, 6:381-384; Halpern, M., Ann. Rev. Neurosci., 1987, 10:325-362; Wysocki, C.J., et al., In the Neurobiology of Taste and Smell, 1987, 125-150; Hildebrand, J.G., et al., Brain Res., 1997, 677:157-161). In mammals, sensory neurons in the nasal olfactory epithelium (OE) detect volatile odorants and some pheromones while those in an -2-

accessory olfactory organ, called the vomeronasal organ (VNO), are thought to be specialized to detect pheromones. The VNO is a tubular structure, at the base of the nasal septum, which is connected to the nasal cavity by a small duct. Signals from the OE are relayed through the olfactory bulb (OB) to the olfactory cortex, and then to multiple brain regions, including those involved in conscious perception. In contrast, signals from the VNO are conveyed through the accessory olfactory bulb (AOB) to the amygdala and hypothalamus, areas associated with the endocrine and behavioral responses induced by pheromones.

Volatile odorants are detected in the OE by as many as 1000 different types of odorant receptors (ORs), which are differentially expressed by olfactory sensory neurons (Buck and Axel, Cell, 1991, 65:175-187; Levy, N.S., et al., J. Steroid Biochem. Mol. Biol., 1991, 39:633-637, 1991; Nef, P., et al., Proc. Natl. Acad. Sci., 1992, 89:8948-8952; Strotman, J., et al., Neuroreport, 1992, 3:1053-1056; Ngai, J., et al., Cell, 1993, 72:667-680; Ressler, K.J., et al., Cell, 1993, 73:597-609; Vassar, R., et al, Cell, 1993, 74:309-318. The ORs are thought to couple to the G protein a subunit, $G\alpha_{oin}$ thereby initiating a cascade of transduction events which culminate in the generation of action potentials in the sensory axons (reviewed in Firestein, S., Curr. Opin. in Neurobiology, 1992, 2:444-448; Reed, R., Neuron, 1992, 8:205-209; Ronnett, G., et al., Trends Neurosci, 1992, 15:508-513). Current evidence suggests that each OR may recognize a particular molecular feature that can be shared by many odorants (Ressler, K., et al., Cell, 1994, 79:1245-1255; Vassar, R., et al., Cell, 1994, 79:981-991; Axel, R., Sci. Am., 1995, 1273:154-159; Buck, L., Annu. Rev. Neurosci., 1996, 19:517-544). This is consistent with a combinatorial coding model in which the identities of different odorants are encoded by different combinations of receptors, but each receptor serves as one component of the codes for many odorants. By contrast, very little is known about how pheromones are detected or encoded in the VNO. Although VNO neurons (VNs) resemble olfactory sensory neurons in the nose, only a rare VN expresses an OR gene. VNs also lack a number of other olfactory sensory transduction molecules, including the G protein a subunit, Ga_{nt} (Reed, R., Neuron, 1992, 8:205-209), which is highly expressed in olfactory neurons (Dulac and Axel, Cell, 1995, 83:195-206; Berghard, A., et al, Proc. Natl. Acad. Sci. USA, 1996, 93:2365-2369; Wu, Y., et al, Biochem. Biopys. Res. Com., 1996, 220:900-904). Instead, VNs express high levels of two other G protein a subunits, $G\alpha_0$ and $G\alpha i_2$ (Dulac and Axel, Cell, 1995, 83:195-206; Halpern, M., Brain Res., 41995, 677:157-161; Berghard, A., et al, Proc. Natl. Acad. Sci. USA, 1996, 93:2365-2369). G_{sp} and Gαi₂ are expressed in spatially-segregated subsets of VNs that form longitudinal zones

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in the VNO neuroepithelium. Interestingly, Dulac and Axel have identified a family of ~ 100 candidate pheromones receptors ("VNRs") which appear to be expressed exclusively in the $G\alpha i_2$ subset (Dulac and Axel, *Cell*, 1995, 83:195-206).

This invention differs from the state of the art in providing a novel family of mammalian pheromone receptors. Accordingly, the objects of the invention relate to providing compositions containing these novel receptors and their binding partners and methods for using such compositions to modulate pheromone receptor activity.

Summary of the Invention

The invention involves the discovery of a multigene family of mammalian pheromone receptors. In particular, the invention involves the cDNA cloning of multiple pheromone receptors from a murine VNO cDNA library and from a rat VNO cDNA library. Partial sequences of human homologs of these pheromone receptors also are provided.

In general, the invention provides isolated nucleic acid molecules encoding the novel pheromone receptors, unique fragments of the isolated nucleic acid molecules, expression vectors containing the foregoing, and host cells transfected with the foregoing. The invention also provides isolated pheromone receptor polypeptides and agents which bind such polypeptides, including antibodies. The foregoing can be used in the diagnosis or treatment of conditions, including the control of fertility, that are characterized by the expression of a pheromone receptor polypeptide. Methods for identifying pharmacological agents useful in the diagnosis or treatment of such conditions and methods for identifying additional members of this multigene family also are provided.

Applicants have discovered that the pheromone receptors disclosed herein are expressed in the vomeronasal organ (VNO), particularly in $G\alpha_0$ protein expressing neurons. This is in contrast to the prior art VNO pheromone receptors which are expressed in neurons which express different G-coupled proteins ($G\alpha_1$ -expressing neurons). Thus, the novel pheromone receptors disclosed herein are distinct from, and expressly exclude, the prior art VNO pheromone receptors which differ in primary structure, as well as in cell localization. Although Applicants do not intend the invention to be limited to a particular theory or mechanism, the amino acid sequence homology and structural organization of the pheromone receptor polypeptides to other well-known G-protein coupled receptors suggests that the pheromone receptors disclosed herein also are G-protein coupled. Thus, it is anticipated that the binding to the pheromone receptor of its

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cognate ligand (pheromone) will be accompanied by G-protein signal transduction, an event which can be measured using conventional screening assays, such as assays that measure changes in the intracellular concentrations of calcium and/or cyclic nucleotides (see, e.g., PCT publication no. WO 94/18959, entitled "Calcium Receptor-Active Molecules", inventors E. Nemeth et al.).

According to one aspect of the invention, a family of pheromone receptor polypeptides is provided. Each polypeptide of the family shares amino acid sequence homology and structural organization with a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52. Each polypeptide member of the receptor family contains, from amino terminus to carboxyl terminus, the following domains: (a) an amino-terminal extracellular domain containing from 30 to 600 amino acids; (b) a transmembrane region comprising: (i) seven non-contiguous transmembrane domains designated TM1, TM2, TM3, TM4, TM5, TM6 and TM7, (ii) three noncontiguous extracellular domains designated EC2, EC3 and EC4, and (iii) three non-contiguous intracellular domains designated IC1, IC2, and IC3, wherein the transmembrane domains, the extracellular domains and the intracellular domains are attached to one another from amino terminus to carboxyl terminus in the order TM1-IC1-TM2-EC2-TM3-IC2-TM4-EC3-TM5-IC3-TM6-EC4-TM7, and wherein the transmembrane region has at least about 35% homology and a length approximately equal to a transmembrane region of a polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50; and (c) a carboxyl-terminal intracellular domain containing from 5 to 200 amino acids. Each polypeptide member of the family is expressed in a $G\alpha_0$ protein-expressing vomeronasal organ neuron or are expressed in another olfactory organ neuron in an animal which does not possess a vomeronasal organ. One skilled in the art can readily identify olfactory organs in animals which do not possess a vomeronasal organ.

In general, the amino-terminal extracellular domains (NTDs) of the receptor family members share sequence homology to a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, and 50 to a lesser extent than that observed for the transmembrane region. The length of the extracellular domain can vary among members of the family. Accordingly, certain embodiments of the invention have extracellular domains that contain at least 50, 100, 200, 300, 400 or 500 amino acids. Preferably, the transmembrane region has greater than 40% homology

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with the corresponding region of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50, and more preferably, have even greater sequence homology (e.g., more than 50%, 60%, 70%, 80% or 90% homology). The length of the carboxyl-terminal intracellular domain can vary among members of the family. Accordingly, certain embodiments of the invention have carboxyl-terminal intracellular domains that contain at least between 5 and 50 amino acids. More preferably, carboxyl-terminal intracellular domains contain between 15 and 25 amino acids.

According to another aspect of the invention, a method for identifying a nucleic acid encoding a pheromone receptor is provided. The method involves contacting a mixture of nucleic acid molecules (genomic library, cDNA library, genomic DNA, RNA, etc.) with at least one nucleic acid probe of a nucleic acid selected from the group consisting of: (a) a nucleic acid molecule selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55 that encodes a pheromone receptor polypeptide; (b) a unique fragment of (a); (c) a human homolog of (a) or (b); and (d) a set of degenerate primers of any of (a), (b) or (c); and identifying the sequences within the mixture that hybridize to the probe. Selected fragments of human homologs of a pheromone receptor are selected from the group consisting of SEQ ID NO. 51, 53, 54 and 55. In certain embodiments, the nucleic acid probe further includes a detectable label to facilitate identification of the sequence in the library which hybridizes to the probe. In certain embodiments, the probe is represented by a pair of degenerate polymerase chain reaction ("PCR") primers that amplify a unique fragment of a nucleic acid molecule selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55. The meaning of "unique fragment" in reference to a nucleic acid is provided below. By "degenerate PCR primers that amplify a unique fragment" is meant degenerate primers which result in the amplification of a unique fragment following a polymerase chain reaction. According to this embodiment, the method for identifying a nucleic acid encoding a pheromone receptor polypeptide further involves subjecting a mixture of nucleic acids and the degenerate PCR primers to amplification conditions prior to identifying the sequences of the mixture that hybridize to the probe and that form part of the amplification reaction products. In some embodiments the pair of degenerate polymerase chain reaction primers is selected from a conserved sequence motif of a pheromone receptor polypeptide. A "conserved sequence motif" can be determined using the side-by-side comparison of the amino acid sequences of the different

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pheromone receptor polypeptides of the invention. Exemplary conserved sequence motifs include regions selected from the group consisting of amino acids 191-397, amino acids 565-825, amino acids 637-825, amino acids 637-804, amino acids 619-784, of the polypeptide of, for example, SEQ ID NO. 2 (VR1). In preferred embodiments, the pair of degenerate polymerase chain reaction primers is selected from the group consisting of SEQ ID NOs. 60 and 61, SEQ ID NOs. 62 and 63, SEQ ID NOs. 64 and 63, SEQ ID NOs. 64 and 65, and SEQ ID NOs. 66 and 67.

According to yet another aspect of the invention, an isolated nucleic acid molecule is provided. The isolated nucleic acid molecule hybridizes under high or low stringency conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55. The invention further embraces nucleic acid molecules that differ from the foregoing isolated nucleic acid molecules in codon sequence due to the degeneracy of the genetic code. The invention also embraces complements of the foregoing nucleic acids.

The pheromone receptors of the invention are expressed in the vomeronasal organ or, in an animal which lacks such an organ, are expressed in another olfactory organ. More particularly, the receptors of the invention are expressed in a $G\alpha_0$ protein-expressing vomeronasal organ neuron. Although not intending to be bound to a particular mechanism, it is believed that the receptors of the invention are G-protein coupled receptors. This is supported by Applicants' discovery that the receptors of the invention are expressed in $G\alpha_0$ protein-expressing vomeronasal organ neurons.

The pheromone receptors of the invention bind to ligands (pheromones) which induce certain changes in receptor conformation. Methods for identifying ligands which bind to the pheromone receptors of the invention are provided below, e.g., by forming an affinity matrix containing immobilized receptor and using the matrix to isolate a cognate ligand from a complex mixture. The particular ligand bound by a particular receptor is dictated by the primary and secondary structure of the receptor. In certain embodiments, the immobilized pheromone receptor polypeptide is a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.

According to another aspect of the invention, an isolated nucleic acid molecule that is a unique fragment of any of the foregoing isolated nucleic acid molecules is provided. In general, the isolated nucleic acid molecule consists of a unique fragment between 12 and 4000

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nucleotides in length, and complements thereof, of any cDNA (SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55) encoding a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52. 5 Depending upon its intended use (e.g., probe, primer), the unique fragment can be between 12 and 2000, 1000, 500, 250, 100, 50 or 25 nucleotides in length. Preferably, the isolated nucleic acid molecule consists of between 12 and 35 contiguous nucleotides of the foregoing cDNAs encoding the pheromone receptor polypeptides, or complements of such nucleic acid molecules. More preferably, the unique fragment is at least 14, 15, 16, 17, 18, 20 or 22 contiguous nucleotides of the nucleic acid sequence of the foregoing cDNAs encoding the pheromone receptor polypeptides, or complements thereof. Particularly preferred isolated nucleic acid molecules are isolated fragments of the foregoing cDNAs which encode one or more of the following pheromone receptor polypeptide domains, alone or in combination (e.g., as fusion proteins): an amino-terminal extracellular domain, a transmembrane region, and a carboxyterminal intracellular domain. In certain embodiments, the unique fragments are a pheromone receptor extracellular domain or a pheromone receptor intracellular domain coupled to at least one (e.g., 1, 2, 3, 4, 5, 6, or 7) transmembrane domain.

According to yet another aspect of the invention, an isolated nucleic acid molecule comprising a molecule having a sequence selected from the group consisting of SEQ ID NO. 51, 53, 54, 55, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, and 92, that encodes a pheromone receptor polypeptide are provided. This aspect of the invention further embraces nucleic acid molecules that differ from these nucleic acid molecules in codon sequence due to the degeneracy of the genetic code, and diversity among pheromone receptors and complements of foregoing.

According to still other aspects of the invention, an expression vector comprising any of the foregoing isolated nucleic acid molecules operably linked to a promoter and host cells transformed or transfected with the same also are provided.

According to another aspect of the invention, an isolated polypeptide encoded by any of the above-described isolated nucleic acid molecules is provided. Preferably, the isolated polypeptide is a pheromone receptor polypeptide that has a pheromone receptor activity or an antigenic fragment thereof. As used herein, a pheromone receptor activity refers to the ability of the pheromone receptor to selectively bind to its cognate ligand (pheromone) and, optionally,

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upon binding, to induce signal transduction in a cell that expresses the pheromone receptor. In preferred embodiments, the isolated polypeptide comprises a pheromone receptor polypeptide having a sequence selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.

According to yet other embodiments, the isolated polypeptide comprises a polypeptide encoded by a nucleic acid which hybridizes under high or low stringency conditions to the extracellular domain, transmembrane region and/or intracellular domain of a cDNA sequence selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55 that encodes a pheromone receptor polypeptide or fragment thereof. Thus, the invention embraces portions of a pheromone receptor polypeptide that may include, for example, an amino-terminal extracellular domain or a carboxyterminal intracellular domain coupled to 1, 2, 3, 4, 5, 6, or 7 transmembrane domains. Preferably, such polypeptides or fragments thereof are unique fragments and can function as, for example, antigens for making antibodies specific for pheromone receptor family members. 15 Accordingly, the polypeptides of the invention can be used to isolate additional members of the pheromone receptor family or, alternatively, can be used to induce in vivo an immune response to a pheromone receptor, i.e., can be incorporated into a vaccine preparation. Such vaccine compositions are useful for controlling fertility or behavior in an animal by administering to the animal, an effective amount of the vaccine to elicit an immune response to the pheromone receptor. Thus, the invention embraces fragments or variants of the foregoing pheromone receptors which exhibit certain detectable activities, e.g., a ligand binding activity, an antigenicity activity. In certain embodiments, the isolated polypeptide is encoded by a cDNA selected from the group consisting of SEQ ID NO. 51, 53, 54, 55, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, and 92, that encodes a pheromone receptor polypeptide or one or more of its domains.

According to another aspect of the invention, there are provided isolated binding polypeptides which selectively bind a unique amino acid sequence of a pheromone receptor polypeptide or fragment thereof. The isolated binding polypeptide in certain embodiments binds to a polypeptide comprising the extracellular domain and/or 1, 2, 3, 4, 5, 6, or 7 transmembrane domains of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.

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The isolated polypeptide preferably binds to a polypeptide consisting of the aminoterminal extracellular domain and/or one or more portions of the transmembrane region of a pheromone receptor polypeptide sequence selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52. In preferred embodiments, isolated binding polypeptides include antibodies and fragments of antibodies (e.g., Fab, F(ab)₂, Fd and antibody fragments which include a CDR3 region which binds selectively to the unique sequences of the polypeptides of the invention). In the preferred embodiments, the isolated binding peptides do not bind to pheromone receptors that are expressed in vomeronasal organ neurons other than Gαo-protein-expressing neurons.

The invention provides in yet other aspects, isolated nucleic acids or polypeptides of the invention that are: (a) immobilized to an insoluble support (an affinity matrix containing immobilized pheromone receptor polypeptide or a unique fragment thereof); (b) associated with, covalently coupled to, or encapsulated a drug delivery device (e.g., a microsphere) to effect controlled release of the isolated nucleic acid or polypeptide in vivo or in vitro; (c) covalently coupled to another isolated nucleic acid or protein to form a chimeric molecule; and/or (d) labeled with a detectable agent (e.g., a radiolabel, a fluorescent label). Thus, the invention provides chimeric molecules containing at least one first structural domain of one pheromone receptor polypeptide (e.g., an extracellular domain) coupled to a second structural domain (e.g., a transmembrane domain, such as TM1, TM2, etc.) of a different pheromone receptor polypeptide. The invention also provides a method for isolating a pheromone receptor by (1) contacting a composition containing a putative pheromone receptor of the above-described family with an affinity matrix containing immobilized binding polypeptide under conditions to permit the pheromone receptor to selectively bind to the immobilized binding polypeptide, and (2) isolating the polypeptides that bind to the affinity matrix.

According to still another aspect of the invention, pharmaceutical compositions containing any of the foregoing compounds of the invention in a pharmaceutically acceptable carrier and methods of producing same by placing the compositions in the carrier also are provided.

According to still another aspect of the invention, methods for modulating a pheromone receptor activity (e.g., a ligand binding activity, a signal transduction activity) in a cell (vertebrate or invertebrate) are provided. The cell can be located in vivo or in vitro and the methods can be used to down regulate (inhibit) or up regulate (stimulate) the pheromone receptor

activity. For example, to inhibit a ligand binding activity, the cell is contacted with an inhibitor that can be an isolated binding polypeptide that binds to an extracellular portion of the receptor and, thereby, inhibits receptor binding to its cognate ligand. Such binding also can induce conformational changes in the receptor that alter the signal transduction activity of the receptor.

conformational changes in the receptor that alter the signal transduction activity of the receptor. The inhibitor can be an isolated antibody (or function equivalent thereof) which binds to an epitope located on an extracellular portion (such as EC2, EC3, EC4) of the pheromone receptor polypeptide, e.g., an amino-terminal extracellular domain or an "extracellular transmembrane region domain", i.e., an extracellular portion of the transmembrane region located between one or more transmembrane domains. Alternatively, the inhibitor can be an agent (e.g., an isolated competitive binding polypeptide) that inhibits receptor-ligand binding. For example, the inhibitor can be an isolated fragment of a pheromone receptor (preferably, a soluble fragment), which fragment contains a ligand (pheromone) binding site. Other inhibitors can be identified in screening assays which test the ability of a putative inhibitor to inhibit pheromone receptormediated signal transduction or which test the ability of the putative inhibitor to inhibit binding of a pheromone receptor to its known cognate ligand. Similarly, such screening assays can be used to identify molecules which stimulate pheromone receptor-mediated signal transduction. Exemplary molecules which stimulate transduction include the naturally-occurring ligands (e.g., isolated from a biological source (e.g., urine, vaginal fluid), as well as synthetic ligands obtained from a non-biological source (e.g., a combinatorial library).

According to still another aspect of the invention, methods for inhibiting the binding of a pheromone having a binding domain to a pheromone receptor polypeptide having a ligand binding site that selectively binds to the binding domain are provided. The method involves contacting (in vivo or in vitro) the pheromone receptor polypeptide with an agent which binds to the ligand binding site under conditions to permit binding of the agent to the receptor. For example, the agent can be an isolated binding polypeptide that binds to the ligand binding site of the pheromone receptor. Thus, the agent can be an isolated antibody (or functionally equivalent fragment thereof) which selectively binds to the ligand binding site of the receptor. Alternatively, the agent can be a pheromone receptor antagonist, e.g., a molecule that mimics the structure of the naturally-occurring ligand but that does not mimic the function (stimulating the receptor) of the naturally-occurring ligand. Agents which inhibit ligand binding can be identified in screening assays which test the ability of a putative binding inhibitor to inhibit

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binding of a pheromone receptor to its cognate ligand (e.g., pheromone). Such molecules can be isolated from a biological source or from a non-biological source.

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According to another aspect of the invention, methods for modulating pheromone receptor-mediated signal transduction in a subject are provided. The methods involve administering to a subject in need of such treatment an agent that selectively binds to any of the above-described isolated nucleic acid molecules which encode a pheromone receptor or unique fragment thereof, or an expression product thereof, in an amount effective to modulate (down regulate or up regulate) pheromone receptor-mediated signal transduction in the subject. Exemplary agents include antisense nucleic acid molecules and binding polypeptides.

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Thus, according to yet another aspect of the invention, methods are provided for identifying lead compounds for an pharmacological agent useful in the diagnosis or treatment of a condition associated with pheromone receptor signal transduction activity or otherwise generally associated with binding of the receptor to its cognate ligand. Preferably, cells expressing intact pheromone receptor polypeptides or portions thereof are used in the screening assays for identifying lead compounds which modulate pheromone receptor-mediated ligand binding or signal transduction activity. Cells expressing these polypeptides, isolated pheromone receptor polypeptides and fragments of these polypeptides which contain the ligand binding site can be used in the screening assays for identifying lead compounds which modulate binding of the receptor to a known ligand.

The screening methods involve forming a mixture of a pheromone receptor polypeptide (as noted above) or fragment thereof containing a ligand binding site; a molecule which is known to (1) interact with the foregoing receptor to effect pheromone receptor-mediated signal transduction or (2) bind to the ligand binding site of the receptor; and a candidate pharmacological agent. The mixture is incubated under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of pheromone receptor-ligand binding or receptor-mediated signal transduction by the known ligand. A test amount of the selective binding of the ligand by receptor or of the specific activation of signal transduction is determined. Detection of an increase in the foregoing activities in the presence of the candidate pharmacological agent indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases specific activation of pheromone receptor-mediated signal transduction or selective binding of the ligand by the ligand binding site of the receptor. Detection of a decrease in the foregoing activities in the presence of the candidate

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pharmacological agent indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which decreases specific activation of pheromone receptor-mediated signal transduction or selective binding of the ligand by the ligand binding site of the receptor.

Pheromone receptor polypeptides that are useful in the screening assays, preferably, are those selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52. Extracellular domains or portions thereof and portions of the transmembrane region, alone or coupled to one another, of these pheromone receptor polypeptides (indicated in the Examples) can be tested for their ability to inhibit receptor-ligand binding.

These and other objects of the invention will be described in further detail in connection with the detailed description of the invention.

All patents, patent publications, references and other information identified in this document are incorporated in their entirety herein by reference.

Brief Description of the Drawings

Figure 1 depicts a comparison of the deduced protein sequences encoded by VR cDNA clones.

Figure 2 is a schematic comparison of ORs, VNRs, and Vrs.

Figure 3 depicts a comparison of the deduced protein sequences encoded by the 20 Go-VN cDNA clones.

Brief Description of the Sequences

SEQ ID NO. 1 is the nucleotide sequence of the mouse pheromone receptor VR1 cDNA (GenBank Accession No. AF011411).

SEQ ID NO. 2 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR1 cDNA (GenBank Accession No. AF011411).

SEQ ID NO. 3 is the nucleotide sequence of the mouse pheromone receptor VR2 cDNA (GenBank Accession No. AF011412).

SEQ ID NO. 4 is the predicted amino acid sequence of the polypeptide encoded by
the mouse pheromone receptor VR2 cDNA (GenBank Accession No. AF011412).

SEQ ID NO. 5 is the nucleotide sequence of the mouse pheromone receptor VR3 cDNA (GenBank Accession No. AF011413).

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SEQ ID NO. 6 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR3 cDNA (GenBank Accession No. AF011413).

SEQ ID NO. 7 is the nucleotide sequence of the mouse pheromone receptor VR4 cDNA (GenBank Accession No. AF011414).

SEQ ID NO. 8 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR4 cDNA (GenBank Accession No. AF011414).

SEQ ID NO. 9 is the nucleotide sequence of the mouse pheromone receptor VR5 cDNA (GenBank Accession No. AF011415).

SEQ ID NO. 10 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR5 cDNA (GenBank Accession No. AF011415).

SEQ ID NO. 11 is the nucleotide sequence of the mouse pheromone receptor VR6 cDNA (GenBank Accession No. AF011416).

SEQ ID NO. 12 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR6 cDNA (GenBank Accession No. AF011416).

SEQ ID NO. 13 is the nucleotide sequence of the mouse pheromone receptor VR7 cDNA (GenBank Accession No. AF011417).

SEQ ID NO. 14 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR7 cDNA (GenBank Accession No. AF011417).

SEQ ID NO. 15 is the nucleotide sequence of the mouse pheromone receptor VR8 cDNA (GenBank Accession No. AF011418).

SEQ ID NO. 16 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR8 cDNA (GenBank Accession No. AF011418).

SEQ ID NO. 17 is the nucleotide sequence of the mouse pheromone receptor VR9 cDNA (GenBank Accession No. AF011419).

SEQ ID NO. 18 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR9 cDNA (GenBank Accession No. AF011419).

SEQ ID NO. 19 is the nucleotide sequence of the mouse pheromone receptor VR10 cDNA (GenBank Accession No. AF011420).

SEQ ID NO. 20 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR10 cDNA (GenBank Accession No. AF011420).

SEQ ID NO. 21 is the nucleotide sequence of the mouse pheromone receptor VR11 cDNA (GenBank Accession No. AF011421).

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SEQ ID NO. 22 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR11 cDNA (GenBank Accession No. AF011421).

SEQ ID NO. 23 is the nucleotide sequence of the mouse pheromone receptor VR12 cDNA (GenBank Accession No. AF011422).

SEQ ID NO. 24 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR12 cDNA (GenBank Accession No. AF011422).

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SEQ ID NO. 25 is the nucleotide sequence of the mouse pheromone receptor VR13 cDNA (GenBank Accession No. AF011423).

SEQ ID NO. 26 is the predicted amino acid sequence of the polypeptide encoded by
the mouse pheromone receptor VR13 cDNA (GenBank Accession No. AF011423).

SEQ ID NO. 27 is the nucleotide sequence of the mouse pheromone receptor VR14 cDNA (GenBank Accession No. AF011424).

SEQ ID NO. 28 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR14 cDNA (GenBank Accession No. AF011424).

SEQ ID NO. 29 is the nucleotide sequence of the mouse pheromone receptor VR15 cDNA (GenBank Accession No. AF011425).

SEQ ID NO. 30 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR15 cDNA (GenBank Accession No. AF011425).

SEQ ID NO. 31 is the nucleotide sequence of the mouse pheromone receptor VR16 cDNA (GenBank Accession No. AF011426).

SEQ ID NO. 32 is the predicted amino acid sequence of the polypeptide encoded by the mouse pheromone receptor VR16 cDNA (GenBank Accession No. AF011426).

SEQ ID NO. 33 is the nucleotide sequence of the rat pheromone receptor Go-VN1 cDNA (GenBank Accession No. AF016178).

SEQ ID NO. 34 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN1 cDNA (GenBank Accession No. AF016178).

SEQ ID NO. 35 is the nucleotide sequence of the rat pheromone receptor Go-VN2 cDNA (GenBank Accession No. AF016179).

SEQ ID NO. 36 is the predicted amino acid sequence of the polypeptide encoded by
the rat pheromone receptor Go-VN2 cDNA (GenBank Accession No. AF016179).

SEQ ID NO. 37 is the nucleotide sequence of the rat pheromone receptor Go-VN3 cDNA (GenBank Accession No. AF016180).

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SEQ ID NO. 38 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN3 cDNA (GenBank Accession No. AF016180).

SEQ ID NO. 39 is the nucleotide sequence of the rat pheromone receptor Go-VN4 cDNA (GenBank Accession No. AF016181).

SEQ ID NO. 40 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN4 cDNA (GenBank Accession No. AF016181).

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SEQ ID NO. 41 is the nucleotide sequence of the rat pheromone receptor Go-VN5 cDNA (GenBank Accession No. AF016182).

SEQ ID NO. 42 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN5 cDNA (GenBank Accession No. AF016182).

SEQ ID NO. 43 is the nucleotide sequence of the rat pheromone receptor Go-VN6 cDNA (GenBank Accession No. AF016183).

SEQ ID NO. 44 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN6 cDNA (GenBank Accession No. AF016183).

SEQ ID NO. 45 is the nucleotide sequence of the rat pheromone receptor Go-VN7 cDNA (GenBank Accession No. AF016184).

SEQ ID NO. 46 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN7 cDNA (GenBank Accession No. AF016184).

SEQ ID NO. 47 is the nucleotide sequence of the rat pheromone receptor Go-VN13C cDNA (GenBank Accession No. AF016185).

SEQ ID NO. 48 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN13C cDNA (GenBank Accession No. AF016185).

SEQ ID NO. 49 is the nucleotide sequence of the rat pheromone receptor Go-VN13B cDNA (GenBank Accession No. AF016186).

SEQ ID NO. 50 is the predicted amino acid sequence of the polypeptide encoded by the rat pheromone receptor Go-VN13B cDNA (GenBank Accession No. AF016186).

SEQ ID NO. 51 is a partial nucleotide sequence of the human pheromone receptor hVR1.

SEQ ID NO. 52 is the predicted amino acid sequence of the polypeptide encoded by the partial sequence of the human pheromone receptor hVR1.

SEQ ID NO. 53 is a partial nucleotide sequence of the human pheromone receptor hVNO1.

SEQ ID NO. 54 is a partial nucleotide sequence of the human pheromone receptor hVNO2.

SEQ ID NO. 55 is a partial nucleotide sequence of the human pheromone receptor hVNO3.

SEQ ID NO. 56 is the nucleotide sequence of primer AL1.

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SEQ ID NO. 57 is the nucleotide sequence of primer AL3.

SEQ ID NO. 58 is a fifty amino acid sequence of Go-VN13B (SEQ ID NO. 50) that is absent from Go-VN13C (SEQ ID NO. 48).

SEQ ID NO. 59 is the amino acid sequence of a rat kidney extracellular calcium/ polyvalent cation-sensing receptor.

SEQ ID NO. 60 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 61 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 62 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 63 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 64 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 65 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 66 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 67 is a degenerate oligonucleotide primer from a conserved VR domain.

SEQ ID NO. 68 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR1.

SEQ ID NO. 69 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR2.

SEQ ID NO. 70 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR3.

SEQ ID NO. 71 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR4.

SEQ ID NO. 72 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR5.

SEQ ID NO. 73 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR6.

SEQ ID NO. 74 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR7.

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SEQ ID NO. 75 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR8.

SEQ ID NO. 76 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR9.

SEQ ID NO. 77 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR10.

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SEQ ID NO. 78 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR11.

SEQ ID NO. 79 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR12.

SEQ ID NO. 80 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR13.

SEQ ID NO. 81 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR14.

SEQ ID NO. 82 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR15.

SEQ ID NO. 83 is the nucleotide sequence of the coding region of the mouse pheromone receptor VR16.

SEQ ID NO. 84 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN1. 20

SEQ ID NO. 85 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN2.

SEQ ID NO. 86 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN3.

SEQ ID NO. 87 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN4.

SEQ ID NO. 88 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN5.

SEQ ID NO. 89 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN6. 30

SEQ ID NO. 90 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN7.

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SEQ ID NO. 91 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN13C.

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SEQ ID NO. 92 is the nucleotide sequence of the coding region of the rat pheromone receptor GoVN13B.

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Detailed Description of the Invention

The present invention in one aspect involves the cloning of cDNAs encoding several members of a multigene family of pheromone receptors. Complete cDNA sequences for selected murine and rat pheromone receptors are provided. Partial sequences of the human gene also are provided. The present invention also relates to the discovery that this family of pheromone receptors is expressed in a $G\alpha_0$ protein-expressing vomeronasal organ neurons (" $G\alpha$ + VNO") or in another olfactory organ neuron in an animal (preferably, a mammal and more preferably, a human) which lacks a vomeronasal organ. Throughout this description, the pheromone receptors of the invention alternatively are referred to as "pheromone receptors", " $G\alpha_0$ + VNO pheromone receptors" or, simply, " $G\alpha_0$ + VNO receptors".

Analysis of the sequence homology between members of the receptor family by comparison to nucleic acid and protein databases established that the pheromone receptor family has several domains. These include, from amino terminus to carboxyl terminus:

(a) an amino-terminal extracellular domain containing from 30 to 600 amino acids; (b) a transmembrane region comprising: (i) seven non-contiguous transmembrane domains designated TM1, TM2, TM3, TM4, TM5, TM6 and TM7, (ii) three non-contiguous extracellular domains designated EC2, EC3 and EC4, and (iii) three non-contiguous intracellular domains designated IC1, IC2, and IC3, wherein the transmembrane domains, the extracellular domains and the intracellular domains are attached to one another from amino terminus to carboxyl terminus in the order TM1-IC1-TM2-EC2-TM3-IC2-TM4-EC3-TM5-IC3-TM6-EC4-TM7, and wherein the transmembrane region has at least about 35% homology and a length approximately equal to a transmembrane region of a polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50; and (c) a carboxyl-terminal intracellular domain containing from 5 to 200 amino acids. Each polypeptide member of the family is expressed in a $G\alpha_0$ protein-expressing vomeronasal organ neuron or are expressed in another olfactory organ neuron in an animal which does not possess a vomeronasal organ. One skilled in the art can readily identify olfactory organs in animals which do not possess a vomeronasal organ. The homology can be calculated using various, publicly available software tools developed by NCBI (Bethesda, Maryland) that can be obtained through the internet (ftp://ncbi.nlm.nih.gov/pub/). Exemplary tools include the BLAST system. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis can be obtained using the MacVector sequence analysis software (Oxford Molecular Group).

The structure of the $G\alpha_0^+$ VNO pheromone receptors suggests that these receptors are members of the large G protein-coupled receptor superfamily (GPCR). Like other GPCRs, the $G\alpha_0^+$ VNO pheromone receptors exhibit seven hydrophobic stretches ("hydrophobic domains") and are similar in structure to other types of GPCRs, the calcium sensing receptor (CSR Ser. ID No. 59) and the metabotropic glutamate receptors (mGluRs). The CSR and mGluRs are unusual among the GPCRs in that they have extremely long N-terminal extracellular domain (e.g., 557-565 amino acids), a feature that is shared by the pheromone receptors of the invention. Despite this similarity, the receptors of the invention do not share substantial primary structure homology with the CSR and mGluRs. The receptors of the invention also are very different structurally from two other G-protein coupled receptors, the odorant receptors and $G\alpha_{12}^+$ vomeronasal receptors, which share none of the characteristic sequence motifs of the receptors of the invention and, moreover, which have very small (~12-28 amino acids) N-terminal extracellular domains.

The receptors of the invention differ somewhat in amino acid sequence, with regions of relatively high sequence homology. Refer to Examples 1 and 2 for a discussion and illustration of the amino acid sequence homology for the murine and rat $G\alpha_0^+$ VNO receptors, respectively. Other features of these members of the $G\alpha_0^+$ VNO receptor family also are discussed and illustrated in the Examples. For example, signal sequences have been identified for several of the $G\alpha_0^+$ VNO receptors disclosed in the Examples.

Homologs and alleles of the pheromone receptor nucleic acids of the invention can be identified by conventional techniques. Thus, an aspect of the invention is those nucleic acid sequences (SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55) which code for $G\alpha_0^+$ VNO pheromone receptors and which hybridize to a nucleic acid molecule consisting of the coding region of any one $G\alpha_0^+$ VNO pheromone receptor selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52, under high or low stringency conditions. The term "high or low stringency conditions" as used herein refers to parameters with which the art is familiar. Nucleic acid hybridization parameters may be found

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in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. More specifically, high stringency conditions, as used herein, refers, for example, to hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH₂PO₄(pH7), 0.5% SDS, 2mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. Low stringency conditions would be the same, but with a lower temperature (e.g., 55°C). After hybridization, the membrane upon which the DNA is transferred is washed at 2 x SSC at room temperature and then at 0.2 x SSC/0.5% SDS at temperatures of up to 65°C. Additional conditions of varying stringency are provided in the Examples.

There are other conditions, reagents, and so forth which can used, which result in a similar degree of stringency. The skilled artisan will be familiar with such conditions, and thus they are not given here. It will be understood, however, that the skilled artisan will be able to manipulate the conditions in a manner to permit the clear identification of homologs and alleles of the $G\alpha_0^+$ VNO pheromone receptor nucleic acids of the invention. The skilled artisan also is familiar with the methodology for screening cells and libraries for expression of such molecules which then are routinely isolated, followed by isolation of the pertinent nucleic acid molecule and sequencing.

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In general homologs and alleles typically will share at least 35% nucleotide identity and/or at least 50% amino acid identity to the cDNAs encoding a $G\alpha_0^+$ VNO pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52, in some instances will share at least 50% nucleotide identity and/or at least 65% amino acid identity and in still other instances will share at least 60% nucleotide identity and/or at least 75% amino acid identity. Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention. As discussed above in the Summary of the invention, certain domains within the pheromone receptors may share even greater sequence homology to a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.

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In screening for $G\alpha_0^+$ VNO pheromone receptor polypeptides, a Southern blot may be performed using the foregoing conditions, together with a radioactive probe. After washing the membrane to which the DNA is finally transferred, the membrane can be placed against X-ray film to detect the radioactive signal.

The invention also includes degenerate nucleic acids which include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Thus, it will be apparent to one of ordinary skill in the art that any of the serine-encoding nucleotide triplets may be employed to direct the protein synthesis apparatus, in vitro or in vivo, to incorporate a serine residue into an elongating $G\alpha_0^+$ VNO pheromone receptor polypeptide. Similarly, nucleotide sequence triplets which encode other amino acid residues include, but are not limited to,: CCA, CCC, CCG and CCT (proline codons); CGA, CGC, CGG, CGT, AGA and AGG (arginine codons); ACA, ACC, ACG and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus, the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code. In addition, areas of high similarity among pheromone receptors may differ in amino acid sequences such that they share many, but not all, amino acids. Their nucleotide sequences all differ accordingly.

The invention also provides isolated unique fragments of the cDNAs encoding a $G\alpha_0^+$ VNO polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52, or complements of these sequences. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules outside of the $G\alpha_0^+$ VNO pheromone receptor nucleic acids defined above. Unique fragments can be used as probes in Southern blot assays to identify such nucleic acids, or can be used as primers in amplification assays such as those employing PCR. As known to those skilled in the art, large probes such as 200 nucleotides or more are preferred for certain uses such as Southern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, as demonstrated in the Examples, or for generating immunoassay

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components. Likewise, unique fragments can be employed to produce nonfused fragments of the $G\alpha_0^+$ VNO pheromone receptor polypeptides, useful, for example, in the preparation of antibodies, in immunoassays, and as a competitive binding partner of the pheromones and/or other ligands which bind to the $G\alpha_0^+$ VNO pheromone receptor polypeptides, for example, in therapeutic applications. Unique fragments further can be used as antisense molecules to inhibit the expression of $G\alpha_0^+$ VNO pheromone receptor nucleic acids and polypeptides, particularly for the insecticide and other fertility control purposes as described in greater detail below.

As will be recognized by those skilled in the art, the size of the unique fragment will depend upon its conservancy in the genetic code. Thus, some regions of a cDNA selected from the group consisting of SEQ ID NO. 51, 53, 54, 55, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, and 92, that encodes a $G\alpha_0^+$ VNO polypeptide, and its complement will require longer segments to be unique while others will require only short segments, typically between 12 and 32 nucleotides (e.g. 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 and 32 bases long). Virtually any segment of the region of the cDNAs encoding the full length $G\alpha_0^+$ VNO polypeptide or their complements, that is 18 or more nucleotides in length will be unique. Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from non- $G\alpha_0^+$ VNO pheromone receptor nucleic acids. A comparison of the sequence of the fragment to those on known data bases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed.

As mentioned above, the invention embraces antisense oligonucleotides that selectively bind to a nucleic acid molecule encoding a $G\alpha_0^+$ VNO pheromone receptor polypeptide, to decrease a pheromone receptor activity (e.g., a ligand binding activity, a signal transduction activity). This is desirable in virtually any condition wherein a reduction in pheromone binding or induction of a behavior that is triggered by pheromone binding is desirable, including to control fertility and behavior in vertebrates and invertebrates. The compositions of the invention are particularly useful in, for example, controlling fertility in livestock and controlling reproduction in rodents or insects by interrupting the normal behaviors of rodents or insects that result in reproduction. As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological

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conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions. Based upon the cDNA sequences of Examples 1 and 2 (SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55), or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases which are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., Nature Biotechnol. 14:840-844, 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen which are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to Nterminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., Cell Mol. Neurobiol. 14(5):439-457, 1994) and at which proteins are not expected to bind. Finally, although, Examples 1 and 2 disclose cDNA sequences (SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55), one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of these cDNAs. Thus, the present invention also provides for antisense oligonucleotides which are complementary to the genomic DNA corresponding to a cDNA sequence selected from the group consisting of SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17,

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19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55. Similarly, antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art recognized methods which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness.

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The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphore esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, nucleic acids encoding pheromone receptor polypeptides, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term "physiologically acceptable" refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art.

As used herein, a "vector" may be any of a number of nucleic acids into which a desired sequence may be inserted by restriction and ligation for transport between different genetic environments or for expression in a host cell. Vectors are typically composed of DNA although RNA vectors are also available. Vectors include, but are not limited to, plasmids, phagemids and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector may be cut in a determinable fashion and into which a desired DNA sequence may be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence may occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication may occur actively during a lytic phase or passively during a lysogenic phase. An expression vector is one into which a desired DNA sequence may be inserted by restriction and ligation such that it is operably joined to regulatory sequences and may be expressed as an RNA transcript. Vectors may further contain one or more marker sequences suitable for use in the identification of cells which have or have not been transformed or transfected with the vector. Markers include, for example, genes encoding proteins which increase or decrease either resistance or sensitivity to antibiotics or other compounds, genes which encode enzymes whose activities are detectable by standard assays known in the art (e.g., B-galactosidase or alkaline phosphatase), and genes which visibly affect the phenotype of transformed or transfected cells, hosts, colonies or plaques (e.g., green fluorescent protein).

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Preferred vectors are those capable of autonomous replication and expression of the structural gene products present in the DNA segments to which they are operably joined.

As used herein, a coding sequence and regulatory sequences are said to be "operably" joined when they are covalently linked in such a way as to place the expression or transcription of the coding sequence under the influence or control of the regulatory sequences. If it is desired that the coding sequences be translated into a functional protein, two DNA sequences are said to be operably joined if induction of a promoter in the 5' regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region would be operably joined to a coding sequence if the promoter region were capable of effecting transcription of that DNA sequence such that the resulting transcript might be translated into the desired protein or polypeptide.

The precise nature of the regulatory sequences needed for gene expression may vary between species or cell types, but shall in general include, as necessary, 5' non-transcribed and 5' non-translated sequences involved with the initiation of transcription and translation respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribed regulatory sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined gene. Regulatory sequences may also include enhancer sequences or upstream activator sequences as desired. The vectors of the invention may optionally include 5' leader or signal sequences. The choice and design of an appropriate vector is within the ability and discretion of one of ordinary skill in the art.

Expression vectors containing all the necessary elements for expression are commercially available and known to those skilled in the art. See, e.g., Sambrook et al., *Molecular Cloning:* A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989. Cells are genetically engineered by the introduction into the cells of heterologous DNA (RNA) encoding pheromone receptor polypeptide or fragment or variant thereof. That heterologous DNA (RNA) is placed under operable control of transcriptional elements to permit the expression of the heterologous DNA in the host cell.

Preferred systems for mRNA expression in mammalian cells are those such as pRc/CMV (available from Invitrogen, Carlsbad, CA) that contain a selectable marker such as a gene that

confers G418 resistance (which facilitates the selection of stably transfected cell lines) and the human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1α, which stimulates efficiently transcription *in vitro*. The plasmid is described by Mishizuma and Nagata (*Nuc. Acids Res.* 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (*Mol. Cell. Biol.* 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (*J. Clin. Invest.* 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant is disclosed by Warnier et al., in intradermal injection in mice for immunization against P1A (*Int. J. Cancer*, 67:303-310, 1996).

The invention also embraces so-called expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of each of the previously discussed coding sequences. Other components may be added, as desired, as long as the previously mentioned sequences, which are required, are included.

The invention also permits the construction of pheromone receptor gene "knock-outs" in cells and in animals, providing materials for studying certain aspects of pheromone receptor binding, signal transduction activity, or function.

The invention also provides isolated polypeptides, which include a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52 and unique fragments of these pheromone receptor polypeptides. Such polypeptides are useful, for example, alone or as fusion proteins to generate antibodies.

A unique fragment of a pheromone receptor polypeptide, in general, has the features and characteristics of unique fragments as discussed above in connection with nucleic acids. As will be recognized by those skilled in the art, the size of the unique fragment will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain. Thus, some regions of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52

will require longer segments to be unique while others will require only short segments, typically between 5 and 12 amino acids (e.g. 5, 6, 7, 8, 9, 10, 11 and 12 amino acids long).

Unique fragments of a polypeptide preferably are those fragments which retain a distinct functional capability of the polypeptide. Functional capabilities which can be retained in a unique fragment of a polypeptide include interaction with antibodies, interaction with other polypeptides (G-proteins) or molecules (e.g., a ligand) or fragments thereof, selective binding of nucleic acids or proteins, and enzymatic activity. Those skilled in the art are well versed in methods for selecting unique amino acid sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from non-family members. A comparison of the sequence of the fragment to those on known data bases typically is all that is necessary.

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The invention embraces variants of the pheromone receptor polypeptides described above. As used herein, a "variant" of a pheromone receptor polypeptide is a polypeptide which contains one or more modifications to the primary amino acid sequence of a pheromone receptor polypeptide. Modifications which create a pheromone receptor variant can be made to a pheromone receptor polypeptide 1) to reduce or eliminate an activity of a pheromone receptor polypeptide, such as a ligand binding activity or a signal transduction activity; 2) to enhance a property of a pheromone receptor polypeptide, such as protein stability in an expression system or the stability of protein-protein binding; or 3) to provide a novel activity or property to a pheromone receptor polypeptide, such as addition of an antigenic epitope or addition of a detectable moiety. Modifications to a pheromone receptor polypeptide are typically made to the nucleic acid which encodes the pheromone receptor polypeptide, and can include deletions, point mutations, truncations, amino acid substitutions and additions of amino acids or non-amino acid moieties. Alternatively, modifications can be made directly to the polypeptide, such as by cleavage, addition of a linker molecule, addition of a detectable moiety, such as biotin, addition of a fatty acid, and the like. Modifications also embrace fusion proteins comprising all or part of the pheromone receptor amino acid sequence.

In general, variants include pheromone receptor polypeptides which are modified specifically to alter a feature of the polypeptide unrelated to its physiological activity. For example, cysteine residues can be substituted or deleted to prevent unwanted disulfide linkages. Similarly, certain amino acids can be changed to enhance expression of a pheromone receptor polypeptide by eliminating proteolysis by proteases in an expression system.

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Mutations of a nucleic acid which encode a pheromone receptor polypeptide preferably preserve the amino acid reading frame of the coding sequence, and preferably do not create regions in the nucleic acid which are likely to hybridize to form secondary structures, such a hairpins or loops, which can be deleterious to expression of the variant polypeptide.

Mutations can be made by selecting an amino acid substitution, or by random mutagenesis of a selected site in a nucleic acid which encodes the polypeptide. Variant polypeptides are then expressed and tested for one or more activities to determine which mutation provides a variant polypeptide with the desired properties. Further mutations can be made to variants (or to non-variant pheromone receptor polypeptides) which are silent as to the amino acid sequence of the polypeptide, but which provide preferred codons for translation in a particular host. The preferred codons for translation of a nucleic acid in, e.g., E. coli, are well known to those of ordinary skill in the art. Still other mutations can be made to the noncoding sequences of a pheromone receptor gene or cDNA clone to enhance expression of the polypeptide. The activity of variants of pheromone receptor polypeptides can be tested by cloning the gene encoding the variant pheromone receptor polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the variant pheromone receptor polypeptide, and testing for a functional capability of the pheromone receptor polypeptides as disclosed herein. For example, the variant pheromone receptor polypeptide can be tested for a ligand binding activity, wherein a ligand to which the receptor binds is contacted with the variant receptor and the amount of ligand binding to the variant receptor is determined using conventional procedures to measure the binding of one molecule to another. Preparation of other variant polypeptides may favor testing of other activities, as will be known to one of ordinary skill in the art.

The skilled artisan will also realize that conservative amino acid substitutions may be made in pheromone receptor polypeptides to provide functionally equivalent variants of the foregoing polypeptides, i.e, the variants retain the functional capabilities of the pheromone receptor polypeptides. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring

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Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. To a certain extent, the various members of the pheromone receptor family that are illustrated in the Examples represent exemplary functionally equivalent variants of the pheromone receptor polypeptides. Other functionally equivalent variants include conservative amino acid substitutions of the amino acids of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D.

Conservative amino-acid substitutions in the amino acid sequence of pheromone receptor polypeptides to produce functionally equivalent variants of pheromone receptor polypeptides typically are made by alteration of the nucleic acid encoding pheromone receptor polypeptides. Such substitutions can be made by a variety of methods known to one of ordinary skill in the art. For example, amino acid substitutions may be made by PCR-directed mutation, site-directed mutagenesis according to the method described in Proc. Nat. Acad. Sci. U.S.A. 82: 488-492, 1985, or by chemical synthesis of a gene encoding a pheromone receptor polypeptide. Where amino acid substitutions are made to a small unique fragment of a pheromone receptor polypeptide, such as a ligand binding site peptide, the substitutions can be made by directly synthesizing the peptide. The activity of functionally equivalent fragments of pheromone receptor polypeptides can be tested by cloning the gene encoding the altered pheromone receptor polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the altered pheromone receptor polypeptide, and testing for a functional capability of the pheromone receptor polypeptides as disclosed herein. Peptides which are chemically synthesized can be tested directly for function, e.g., for binding to a ligand to which the unaltered pheromone receptor is known to bind.

The invention as described herein has a number of uses, some of which are described elsewhere herein. First, the invention permits isolation of the pheromone receptor polypeptides of the Examples. A variety of methodologies well-known to the skilled practitioner can be utilized to obtain isolated pheromone receptor molecules. The polypeptide may be purified from cells which naturally produce the polypeptide by chromatographic means or immunological recognition. Alternatively, an expression vector may be introduced into cells to cause production of the polypeptide. In another method, mRNA transcripts may be microinjected or otherwise

introduced into cells to cause production of the encoded polypeptide. Translation of mRNA in cell-free extracts such as the reticulocyte lysate system also may be used to produce polypeptide. Those skilled in the art also can readily follow known methods for isolating pheromone receptor polypeptides. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography and immune-affinity chromatography.

The isolation of the pheromone receptor gene also makes it possible for the artisan to diagnose a disorder characterized by expression of pheromone receptor. These methods involve determining expression of the pheromone receptor gene, and/or pheromone receptor polypeptides derived therefrom. In the former situation, such determinations can be carried out via any standard nucleic acid determination assay, including the polymerase chain reaction as exemplified in the examples below, or assaying with labeled hybridization probes.

The invention also makes it possible to isolate the naturally occurring ligands (pheromones) and other ligands that have a ligand binding domain, namely, by the binding of such molecules to the pheromone receptor polypeptides (or fragments thereof containing a ligand binding site). Binding of the receptors to a ligand can be accomplished by introducing into a biological system in which the proteins bind (e.g., a cell) a molecule that includes a binding domain (putative ligand) in an amount sufficient to detect the binding.

The invention also provides agents such as binding polypeptides which bind to pheromone receptor polypeptides and/or to complexes of pheromone receptor polypeptides and their ligand binding partners. Such binding agents can be used, for example, in screening assays to detect the presence or absence of pheromone receptor polypeptides and complexes of pheromone receptor polypeptides and their ligand binding partners and in purification protocols to isolate pheromone receptor polypeptides and complexes of pheromone receptor polypeptides and their ligand binding partners. Such agents also can be used to inhibit the native activity of the pheromone receptor polypeptides or their ligand binding partners, for example, by binding to such polypeptides, or their binding partners or both.

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The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to pheromone receptor polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')₂ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

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Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of nonspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. Thus, for example, PCT International Publication Number WO 92/04381 teaches the production and use of humanized murine RSV antibodies in which at least a portion of the murine FR regions have been replaced by FR regions of human origin. Such antibodies, including fragments of intact antibodies with antigen-binding ability, are often referred to as "chimeric" antibodies.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')₂, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric F(ab')₂ fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to pheromone receptor polypeptides, and/or complexes of both pheromone receptor polypeptides and their ligand binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the pheromone receptor polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the pheromone receptor polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the pheromone receptor polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the pheromone receptor polypeptides. Thus, the pheromone receptor polypeptides of the invention, or a fragment thereof, can be used to screen peptide

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libraries, including phage display libraries, to identify and select peptide binding partners of the pheromone receptor polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of pheromone receptor and for other purposes that will be apparent to those of ordinary skill in the art.

A pheromone receptor polypeptide, or a fragment which contains the ligand binding site, also can be used to isolate naturally-occurring ligands and other binding partners of the receptors of the invention. For example, an isolated pheromone receptor can be used to isolate ligands that bind to the receptor binding site by immobilizing a receptor (or fragment containing the ligand binding site) on a chromatographic media, such as polystyrene beads, or a filter, and using the immobilized polypeptide to isolate molecules that bind to this affinity matrix in accordance with standard procedures for affinity chromatography.

It will also be recognized that the invention embraces the use of the pheromone receptor cDNA sequences in expression vectors, as well as to transfect host cells and cell lines, be these prokaryotic (e.g., *E. coli*), or eukaryotic (e.g., CHO cells, COS cells, yeast expression systems and recombinant baculovirus expression in insect cells). Especially useful are oocytes, mammalian cells such as mouse, hamster, pig, goat, primate, etc. They may be of a wide variety of tissue types, and include primary cells and cell lines. The expression vectors require that the pertinent sequence, i.e., those nucleic acids described *supra*, be operably linked to a promoter.

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When administered, the therapeutic compositions of the present invention are administered in pharmaceutically acceptable preparations. Such preparations may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, supplementary immune potentiating agents such as adjuvants and cytokines and optionally other therapeutic agents.

The therapeutics of the invention can be administered by any conventional route, including injection or by gradual infusion over time. The administration may, for example, be oral, intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous, or transdermal. When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing antibodies are well known to those of skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding

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capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694-1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing antibody aerosols without resort to undue experimentation. When using antisense preparations of the invention, slow intravenous administration is preferred.

Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like.

The preparations of the invention are administered in effective amounts. An effective amount is that amount of a pharmaceutical preparation that alone, or together with further doses, produces the desired response in the condition being treated, e.g., modifying fertility or pheromone-mediated behaviors that are related to reproduction or aggression. For example, this can involve the use of the compounds of the invention as pesticides to slow or halt insect or rodent behaviors that result in reproduction. Alternatively, this can involve the use of the compounds of the invention as agents for controlling fertility in animals (e.g., livestock, domestic animals), by providing compounds which inhibit or stimulate the behaviors in such animals that result in reproduction or agression. This can be monitored by routine methods, e.g., observing the behavior in the animal (vertebrate or invertebrate) recipient.

The invention also contemplates gene therapy, e.g., to prepare an animal model for studying the conditions and behaviors (e.g., fertility, aggression) that are pheromone receptor-mediated. The procedure for performing ex vivo gene therapy is outlined in U.S. Patent 5,399,346 and in exhibits submitted in the file history of that patent, all of which are publicly available documents. In general, it involves introduction in vitro of a functional copy of a gene into a cell(s) of a subject which contains a defective copy of the gene, and returning the genetically engineered cell(s) to the subject. The functional copy of the gene is under operable control of regulatory elements which permit expression of the gene in the genetically engineered

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cell(s). Numerous transfection and transduction techniques as well as appropriate expression vectors are well known to those of ordinary skill in the art, some of which are described in PCT application WO95/00654. *In vivo* gene therapy using vectors such as adenovirus, retroviruses, herpes virus, and targeted liposomes also is contemplated according to the invention.

The invention further provides efficient methods of identifying pharmacological agents or lead compounds for agents active at the level of a pheromone receptor or pheromone receptor fragment modulatable cellular function. In particular, such functions include ligand binding activity. Generally, the screening methods involve assaying for activation of pheromone receptors or assaying for compounds which interfere with a pheromone receptor activity such as pheromone receptor binding to its cognate ligand. Such methods are adaptable to automated, high throughput screening of compounds. The target therapeutic indications for pharmacological agents detected by the screening methods that block pheromone receptor activity are limited only in that the target cellular function be subject to modulation by alteration of the formation of a complex comprising a pheromone receptor polypeptide or fragment thereof and one or more natural pheromone receptor ligands. Target indications include cellular processes modulated by pheromone receptor signal transduction following receptor-ligand binding.

A wide variety of assays for pharmacological agents are provided, including, labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays, cell-based assays such as two- or three-hybrid screens, expression assays, activation of G-proteins, etc. For example, three-hybrid screens are used to rapidly examine the effect of transfected nucleic acids on the intracellular binding of pheromone receptor or pheromone receptor fragments to specific extracellular targets (e.g., ligands in biological samples, such as urine, vaginal fluid, or in combinatorial libraries).

Pheromone receptor fragments used in the methods, when not produced by a transfected nucleic acid are added to an assay mixture as an isolated polypeptide. The assay can be used to screen putative ligands for their ability to bind to the receptor. Pheromone receptor polypeptides preferably are produced recombinantly, although such polypeptides may be isolated from biological extracts. Recombinantly produced pheromone receptor polypeptides include chimeric proteins comprising a fusion of a pheromone receptor protein with another polypeptide. For example, a polypeptide fused to a pheromone receptor polypeptide or fragment may also provide means of readily detecting the fusion protein, e.g., by immunological recognition or by fluorescent labeling.

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In addition to the pheromone receptor, a screening assay mixture includes a binding partner for the receptor, e.g., a naturally occurring ligand that is capable of binding to the pheromone receptor or, alternatively, is comprised of an analog which mimics the pheromone receptor binding properties of the naturally occurring ligand for purposes of the assay. The screening assay mixture also comprises a candidate pharmacological agent (e.g., a putative receptor agonist or antagonist). Typically, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a different response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration of agent or at a concentration of agent below the limits of assay detection. Candidate agents encompass numerous chemical classes, although typically they are organic compounds. Preferably, the candidate pharmacological agents are small organic compounds, i.e., those having a molecular weight of more than 50 yet less than about 2500, preferably less than about 1000 and, more preferably, less than about 500. Candidate agents comprise functional chemical groups necessary for structural interactions with polypeptides and/or nucleic acids, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups and more preferably at least three of the functional chemical groups. The candidate agents can comprise cyclic carbon or heterocyclic structure and/or aromatic or polyaromatic structures substituted with one or more of the above-identified functional groups. Candidate agents also can be biomolecules such as peptides, saccharides, fatty acids, sterols, isoprenoids, purines, pyrimidines, derivatives or structural analogs of the above, or combinations thereof and the like. Where the agent is a nucleic acid, the agent typically is a DNA or RNA molecule, although modified nucleic acids as defined herein are also contemplated.

Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides, synthetic organic combinatorial libraries, phage display libraries of random peptides, and the like. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant and animal extracts are available or readily produced. Additionally, natural and synthetically produced libraries and compounds can be readily be modified through conventional chemical, physical, and biochemical means. Further, known pharmacological agents may be subjected to directed or random chemical modifications such as

acylation, alkylation, esterification, amidification, etc. to produce structural analogs of the agents.

A variety of other reagents also can be included in the mixture. These include reagents such as salts, buffers, neutral proteins (e.g., albumin), detergents, etc. which may be used to facilitate optimal protein-protein and/or protein-nucleic acid binding. Such a reagent may also reduce non-specific or background interactions of the reaction components. Other reagents that improve the efficiency of the assay such as protease, inhibitors, nuclease inhibitors, antimicrobial agents, and the like may also be used.

The mixture of the foregoing assay materials is incubated under conditions whereby, but for the presence of the candidate pharmacological agent, the pheromone receptor polypeptide specifically binds the cellular binding target, a portion thereof or analog thereof. The order of addition of components, incubation temperature, time of incubation, and other parameters of the assay may be readily determined. Such experimentation merely involves optimization of the assay parameters, not the fundamental composition of the assay. Incubation temperatures typically are between 4°C and 40°C. Incubation times preferably are minimized to facilitate rapid, high throughput screening, and typically are between 0.1 and 10 hours.

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After incubation, the presence or absence of specific binding between the pheromone receptor polypeptide and one or more binding targets is detected by any convenient method available to the user. For cell free binding type assays, a separation step is often used to separate bound from unbound components. The separation step may be accomplished in a variety of ways. Conveniently, at least one of the components is immobilized on a solid substrate, from which the unbound components may be easily separated. The solid substrate can be made of a wide variety of materials and in a wide variety of shapes, e.g., microtiter plate, microbead, dipstick, resin particle, etc. The substrate preferably is chosen to maximum signal to noise ratios, primarily to minimize background binding, as well as for ease of separation and cost.

Separation may be effected for example, by removing a bead or dipstick from a reservoir, emptying or diluting a reservoir such as a microtiter plate well, rinsing a bead, particle, chromatographic column or filter with a wash solution or solvent. The separation step preferably includes multiple rinses or washes. For example, when the solid substrate is a microtiter plate, the wells may be washed several times with a washing solution, which typically includes those components of the incubation mixture that do not participate in specific bindings such as salts,

buffer, detergent, non-specific protein, etc. Where the solid substrate is a magnetic bead, the beads may be washed one or more times with a washing solution and isolated using a magnet.

Detection may be effected in any convenient way for cell-based assays such as two- or three-hybrid screens. The transcript resulting from a reporter gene transcription assay of Pheromone receptor polypeptide binding to a target molecule typically encodes a directly or indirectly detectable product, e.g., \(\beta\)-galactosidase activity, luciferase activity, and the like. A wide variety of cell based assays for G-protein coupled receptors could also be employed for detection of molecules that stimulate (agonsists) pheromone receptors or block (agonists) that stimulation by natural ligands or agonists. Pheromone receptor polypeptides or chimeric receptors composed only in-part of a pheromone receptor could be employed in these assays. The chimeric receptors might, for example, contain part of another G-protein coupled receptor such that binding of a ligand to the pheromone receptor binding domain results in coupling to a particular G-protein where activation could be easily assayed. For cell free binding assays, one of the components usually comprises, or is coupled to, a detectable label. A wide variety of labels can be used, such as those that provide direct detection (e.g., radioactivity, luminescence, optical or electron density, etc). or indirect detection (e.g., epitope tag such as the FLAG epitope, enzyme tag such as horseradish peroxidase, etc.). The label may be bound to a pheromone receptor binding partner (ligand), or incorporated into the structure of the binding partner.

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A variety of methods may be used to detect the label, depending on the nature of the label and other assay components. For example, the label may be detected while bound to the solid substrate or subsequent to separation from the solid substrate. Labels may be directly detected through optical or electron density, radioactive emissions, nonradioactive energy transfers, etc. or indirectly detected with antibody conjugates, strepavidin-biotin conjugates, etc. Methods for detecting the labels are well known in the art.

The invention provides pheromone receptor -specific binding agents, methods of identifying and making such agents, and their use in diagnosis, therapy and pharmaceutical development, including the development of pesticides and other agents for controlling fertility and reproduction (or related behaviors) in animals. For example, pheromone receptor-specific pharmacological agents are useful in a variety of diagnostic and therapeutic applications, especially where disease or disease prognosis is associated with improper utilization of a pathway involving pheromone receptor. Novel pheromone receptor-specific binding agents include pheromone receptor-specific antibodies and other natural intracellular binding agents

identified with assays such as two hybrid screens, and non-natural intracellular binding agents identified in screens of chemical libraries and the like.

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In general, the specificity of pheromone receptor binding to a binding agent is shown by binding equilibrium constants. Targets which are capable of selectively binding a pheromone receptor polypeptide preferably have binding equilibrium constants of at least about 10⁷ M⁻¹, more preferably at least about 10⁸ M⁻¹, and most preferably at least about 10⁹ M⁻¹. The wide variety of cell based and cell free assays may be used to demonstrate pheromone receptor specific binding. Cell based assays include one, two and three hybrid screens, assays in which pheromone receptor -mediated transcription is inhibited or increased activation of G-proteins, etc. Cell free assays include pheromone receptor -protein binding assays, immunoassays, etc. Other assays useful for screening agents which bind pheromone receptor polypeptides include fluorescence resonance energy transfer (FRET), and electrophoretic mobility shift analysis (EMSA).

Various techniques may be employed for introducing nucleic acids of the invention into cells, depending on whether the nucleic acids are introduced in vitro or in vivo in a host. Such techniques include transfection of nucleic acid-CaPO₄ precipitates, transfection of nucleic acids associated with DEAE, transfection with a retrovirus including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. For example, where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

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Examples

Example 1

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Experimental Procedures

5 Preparation and analysis of single cell cDNAs

Male mouse (C57BL/6J) VNOs were minced, incubated in Trypsin-EDTA (Gibco-BRL/LTI, Rockville, Maryland), and triturated to obtain dissociated cells. The cells were centrifuged (1000 RPM, 5 min) and resuspended in phosphate buffered saline + 0.1% bovine serum albumin. Individual cells that appeared to be neurons were transferred to separate tubes with a microcapillary pipet.

cDNAs were prepared from each cell and amplified according to Brady and Iscove (Methods in Enzymology, 1993, 225:611-621) with minor modifications. Briefly, cDNAs were prepared from the 3' ends of mRNAs by reverse transcription with an oligo (dT) primer, and a poly dA stretch was added to each cDNA with terminal transferase. The cDNAs were then amplified by PCR with one of two primers, AL1 (ATTGGATCCAGGCCGCTCTGGACAA AATATGAA TTC(T) (SEQ. ID. No. 56) (Dulac and Axel, Cell, 1995, 83:195-206 or AL3 (GGCACATGG ACGAAATCTTGGTACTCTTCAGAATTC(T), (SEQ. ID. No. 57) and Taq polymerase [Amplitaq LD ("ALD") or Amplitaq Stoffel Fragment ("ASF") (Perkin Elmer, Norwalk, CT)].

Aliquots of each cDNA sample were electrophoresed on agarose gels and blotted onto nylon membranes (Hybond N⁺, Amersham, Piscataway, NJ) (Ausubel, F., et al., *Current Protocols in Molecular Biology*, 1988, John Wiley & Sons NY, NY; Sambrook, J., et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989). The blots were hybridized at 55° or 70°C in Hyb Buffer (0.5M sodium phosphate buffer (pH7.3), 4% SDS, 1% bovine serum albumin (BSA)) with ³²P-labeled probes prepared by random priming (Prime-It II, Stratagene, La Jolla, CA).

Construction and screening of single cell cDNA libraries

An aliquot of cDNA sample VN14 was digested with Eco RI and gel-isolated fragments of 0.1-1.5 kb were cloned into λZapII Ausubel, F., et al., Current Protocols in Molecular Biology, 1988, John Wiley & Sons NY, NY; Sambrook, J., et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989). Two

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thousand library clones were plated at low density. Replica filter lifts were hybridized at 75°C (in Hyb Buffer containing 2µg/ml poly (dT)24 and 1µg/ml of random dA-dT 20-mers) to ³²P-labeled probes (~2.5 x 10⁸ CPM/µg; 5 x 10⁶ CPM/ml) prepared by PCR of different single cell cDNA samples. Clones that hybridized to only a VN14 probe were isolated, and a probe prepared from the insert of each was hybridized to blots of selected single cell cDNAs. Clones that hybridized to only VN14 cDNAs were sequenced.

Isolation and analysis of VR cDNA clones

sc153, one VN14*VN2* clone from the VN14 library, was used as probe to screen a mouse VNO cDNA library ('λVNO') (Berghard, A., et al., *J Neurosci*, 1996, 16:909-918) and a mouse genomic DNA library (Stratagene, La Jolla, CA) (70°C, Hyb buffer). Hybridizing clones were found only in the genomic library. A fragment containing 2kb upstream of sc153 was isolated from one genomic clone (153G1) and used to screen IVNO (55°C, Hyb Buffer). The region (D10-TM7) of one clone (D10) that showed homology to TM7 of the CSR (SEQ ID NO. 59) was then used to screen IVNO (55°C, Hyb Buffer), yielding a variety of VR cDNA clones. Additional clones were obtained from IVNO using probes prepared from clones previously isolated, or from PCR products obtained by amplification of mouse genomic DNA or VNO cDNA with degenerate primers (Buck, L., et al., *Cell*, 1991, 65:175-187) matching conserved motifs in the VRs. Some PCR products were also cloned into pCR2.1 (Invitrogen, Carlsbad, CA) and sequenced.

Analysis of VR mRNAs by RT-PCR

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Random-primed cDNA prepared from male or female C57BL/6J mouse VNO RNAs (or VR cDNA clones) were used in PCR reactions with degenerate primers (Buck and Axel, *Cell* 1991, 65:175-187) matching conserved VR motifs to amplify VR sequences corresponding to amino acids 33-772 in VR1 (SEQ ID NO. 2). Nested PCR was performed with a 1/1000 dilution of the first PCR reaction and primer pairs matching regions of putative exons 1 and 6 in specific VR cDNA clones. Blots prepared from size-fractionated, nested PCR products were hybridized (70°C, Hyb buffer containing 100µg/ml herring sperm DNA (Sigma, St Louis, MO)) to probes prepared from the PCR products of the cDNA clones.

Northern and Southern bl ts and genomic library screens

Northern Blots: One μg of PolyA⁺ RNA prepared from mouse VNO and OE, or purchased from Clontech (other tissue RNAs), was size fractionated on formaldehyde gels, and blotted (see above) (Berghard and Buck, *J. Neurosci*, 1996, 16:909-918). The blot was hybridized (70°C, Hyb Buffer) with a ³²P-labeled probe prepared from the regions of cDNAs VR1, VR2, VR4, and VR15 corresponding to that encoding amino acids 33-772 in VR1 (SEQ ID NO. 1).

Southern Blots: 5 μg of genomic DNA prepared from C57BL6/J mouse liver was digested with Eco RI or Hind III, size fractionated, and blotted (Ressler et al, *Cell*, 1993, 73:597-609). The blots were hybridized (70°C, Hyb buffer containing sperm DNA (see above)) to probes prepared from 3' untranslated segments of different VR cDNA clones [VR2 (nt.2607-2961 of SEQ ID NO. 3), VR3 (nt. 2505-2907 of SEQ ID NO. 5), and VR15 (nt. 3239-3689 of SEQ ID NO. 29)]. A VR4 probe was also used, which gave the same results as highly related VR15 probe.

Genomic library screens to determine VR gene number: A mouse genomic library was screened separately at 70°C or 55°C (see above) with different ³²P-labeled probes. Probe 1: a mix of segments of cDNAs VR1 (SEQ ID NO. 1), VR2 (SEQ ID NO. 3), VR4 (SEQ ID NO. 7), and VR15 (SEQ ID NO. 29) encoding the region corresponding to amino acids 619-772 of VR1 (SEQ ID NO. 2). Probes 2-6: Segments of VR genes obtained from mouse genomic DNA by PCR with degenerate primers matching conserved VR sequence motifs. The PCR segments corresponded to the following amino stretches in VR1 (SEQ ID NO. 2): amino acids 191-397, 565-825, 637-825, 637-804, and 619-784. For example, degenerate oligonucleotide primer pairs used included:

for amino acids 191-397:

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5' primer= (GCT)TI(CT)A(CT) CA(AG)(AG)TIGCI(AC)CIAA(AG)GA(CT)AC (SEQ ID NO. 60),

3' primer= G(CT)(AG)T(GT)IGCI(AG)(CT)I(AG)C(AG)T(AG)IACI(AG)C(AG)TT (SEQ ID NO. 61);

for amino acids 565-825:

5' primer=(AC)(AG)ITG (CT)CCI(GT)AIIA(CT)(AC)A(AG)TA(CT)GCIAA (SEQ ID NO. 62),

3' primer= GIC(GT)IA(CT)IA(AG)IATIA (CT)(AG)TAI(AC)(AT)(CT)TTIGGIAC (SEQ ID NO. 63);

for amino acids 637-825:

5' primer= ATI(AT)(GC)I (CT) TI(AG)TITT(CT)TG(CT)TT(CT)(CT)TITG (SEQ ID NO. 64), 3' primer= GIC(GT)IA(CT)IA(AG)IATIA (CT)(AG)TAI(AC)(AT)(CT)TTIGGIAC (SEQ ID NO. 63);

for amino acids 637-804:

5' primer= ATI(AT)(GC)I(CT)TI(AG)TITT(CT)TG(CT)TT(CT)(CT)TITG (SEQ ID NO. 64), 3' primer=(AG)IATI(GC)(AT)(AG)AAIA(CT)(CT)TCIACI (AG)CIACCAT (SEQ ID NO. 65); and

for amino acids 619-784:

5' primer= GA(CT)ACICCIATIGTIAA(AG)GCIAA(CT)AA (SEQ ID NO. 66), 3' primer= AAIGTIA(CT)CCAIACI(GC)(AT)(AG)CA(AG)AAIAC (SEQ ID NO. 67), wherein all primers are in a 5'-3' direction, I:Inosine.

In situ hybridization

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In situ hybridization was performed according to Schaeren-Wiemers and Gerfin-Moser (Histochemistry, 1993, 100:431-440) with sequential 16 micron sections of male or female VNOs. Digoxigenin-labeled cRNA probes were prepared from the same 3' untranslated regions of VR cDNAs as used for the genomic Southern blots. Sections were counter-stained with Hoechst 33258, which labels nuclei. The numbers of G_{ac} or G_{ai}-labeled cells (or cells labeled with VR probes) was determined by counting the number of nuclei in labeled regions. The total number of cells was considered to be the sum of G₁₀+ and G₁₂+ cells in adjacent sections.

Chromosome mapping of VR genes

Southern blots of genomic DNA from C57BL/6J and Mus spretus (Jackson Labs) digested with different restriction enzymes were prepared and probed with specific VR cDNA probes as described above. Southern blots of Eco RI, size fractionated genomic DNAs from 94 different backcross mice (M. spretus x (M. spretus x C57BL/6J), were purchased from Jackson Labs. These blots were hybridized to probes prepared from 3' untranslated segments of the VR2 or VR4 (see above) cDNA at 70°C and washed (see above). Polymorphic bands were typed as 30 either M. spretus or M. spretus/C57BL/6J. The data was sent to the Jackson Laboratory Backcross DNA Mapping Panel Resource for determination of the chromosomal locations of the 5

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polymorphic fragments. Additional information was obtained via internet from Jackson Laboratory Mouse Genome Informatics.

Cloning of a gene differentially expressed in Gas+ VNs

Different members of the OR and VNR families are expressed in different neurons in the OE and G_{si2}+ zone of the VNO, respectively. It therefore appeared likely that the same would be true of sensory receptors expressed by G_{sc}+ VNs. The differential screening of cDNA libraries with cDNA probes prepared from a few neurons can be used to identify genes expressed in one neuron, but not another (Buck, L., et al, *Annu. Rev. Neurosci.*, 1996, 19:517-544). Using PCR, this can be accomplished with single cells (Brady, G., et al., *Methods in Enzymology*, 1993, 225:611-621; Dulac, C., et al., *Cell*, 1995, 83:195-206).

To search for genes encoding receptors expressed by G_{ao} + VNs, we looked for genes expressed in one G_{ao} + VN, but not another, using the PCR-based differential screening approach. In initial experiments, we isolated a series of mouse VNs, prepared cDNAs from the 3' ends of mRNAs present in each, and amplified the single-cell cDNA fragments by PCR. Many of the amplified, single-cell cDNA samples hybridized to an OMP probe, confirming their derivation from VNs (Berghard et al, *Proc. Natl. Acad. Sci. USA*, 1996, 93:2365-2369). With one exception, G_{ao} and G_{ai2} probes hybridized to different OMP+ samples, allowing us to identify samples that were derived from G_{ao} + VNs.

We next prepared a library from one of the $G_{\infty}+$ single-cell cDNA samples (VN14), and isolated clones that hybridized to a probe prepared from VN14, but not to a probe prepared from another $G_{\infty}+$ sample (VN2). We identified 3 VN14+VN2- clones, which differed in size, but were otherwise identical in sequence. None contained an open reading frame, which was not surprising since, in the method used, the amplified cDNAs are only ~400-800 bp long, and are derived from the 3' ends of mRNAs (Brady and Iscove, *Methods in Enzymology*, 1993, 225:611-621).

We next hybridized one of the VN14+VN2- clones (sc153) to the original panel of single-cell cDNAs. sc153 hybridized to VN14, but not to any of the other cDNA samples. Consistent with this result, sc153 hybridized to only a small percentage (~0.3%) of VNs in VNO tissue sections.

Using sc153 as probe, we were able to isolate a sc153+ clone from a mouse genomic library which contained ~2 kb of DNA 5' to the sc153 sequence. Using this 2kb fragment as

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probe, we isolated a matching clone (D10) from the VNO cDNA library. Sequence analysis showed that sc153 and D10 were derived from the same gene, but that the D10 cDNA was truncated at the 3' end and did not contain the final 685 bp of sequence present in sc153. Like sc153, D10 hybridized to only a small percentage of VNs in VNO tissue sections.

The 5' end of the D10 cDNA contained a short open reading frame, which encoded a protein fragment with homology to transmembrane domain 7 (TM7) of the calcium sensing receptor (CSR), a G protein-coupled receptor (GPCR) (Brown et al, *Nature*, 1993, 366:575-580). When the TM7-related region of D10 (D10-TM7) was hybridized at reduced stringency (55°C) to the original panel of single-cell cDNAs, it labeled many of the G_{ω} + samples, but none of G_{ω} + ones (except the one that was also G_{ω} +, and was probably derived from two cells). Since D10 labeled only a small percentage of VNs in tissue sections under high stringency conditions, this suggested that many G_{ω} + neurons express a gene related to D10, but not identical to it.

A novel multigene family encoding VNO receptors

Hybridization of D10-TM7 to the VNO cDNA library at reduced stringency yielded a number of related cDNA clones (e.g. VR1-VR3, SEQ ID NOs. 1-6). Additional related cDNAs were obtained by RT-PCR with degenerate primers (e.g. VR6-VR7, SEQ ID NOs. 11-14), or by screening the VNO cDNA library with a PCR product obtained from genomic DNA (e.g., VR4, VR5, SEQ ID NOs. 7-10).

These cDNAs encode a novel family of proteins, which are members of the G protein-coupled receptor (GPCR) superfamily (Figure 1). Like other GPCRs, these VNO receptors (VRs) have 7 hydrophobic stretches that may serve as membrane spanning domains. Only 287 of 850 residues are identical in all of the molecules shown in Figure 1, indicating that the family is diverse. The VRs are related to two other types of GPCR, the calcium sensing receptor (CSR) and the metabotropic glutamate receptors (mGluRs) (Tanabe, Y., et al., *Neuron*, 1992, 8:169-179; Brown, E., et al., *Nature*, 1993, 366:575-580). The most highly related molecule is the CSR; for example, VR1 is 31% identical to rat CSR (Riccardi et al., *Proc. Natl. Acad. Sci. USA*, 1995, 92:131-135), with the highest homology residing in the TM1-TM7 region (44%) (Figure 1). However, the VRs comprise a distinct family of receptors, which share novel sequence motifs, and are more related to one another than they are to other receptors. For example, two divergent VRs, VR1 (SEQ ID NO. 1, 2) and VR4 (SEQ ID NO. 7, 8), are 70% identical in TM1-TM7, and 48% identical overall.

The VRs are unusual among GPCRs in having an extremely long N-terminal extracellular domain (Figures 1 and 2). This feature is shared by the CSR and mGluRs, and by an unrelated class of GPCRs that includes several receptors for glycoprotein hormones (Segaloff, D., et al., Oxf. Rev. Reprod. Biol., 1992, 14:141-168). Importantly, the VRs are very different from both ORs and VNRs, which are also GPCRs (Buck. L., et al., Cell, 1991 51:127-133; Dulac, C., et al., Cell, 1995, 83:195-206). VRs share none of the characteristic sequence motifs of ORs or VNRs. In addition, the size of the N-terminal extracellular domain of VRs (557-565 amino acids) far exceeds that of ORs and VNRs (~12-28 amino acids) (Figure 2). The VRs are most variable in the N-terminal domain (25% identical residues compared to 57% in TM1-TM7). In the structurally-related mGluRs, the ligand binding site is thought to reside in the large N-terminal domain (O'Hara et al., Neuron, 1993, 11:41-52; Takahashi et al, J. Biol. Chem., 1993, 268:19341-19345). If this is also true of VRs, the accentuated diversity of the N-terminal domain may reflect an ability to recognize diverse pheromonal ligands.

Most of the VR cDNAs that we analyzed appeared to belong to one of three subfamilies of highly related molecules. For example, VR1 (SEQ ID NOs. 1, 2), VR2 (SEQ ID NOs. 3, 4), and VR3 (SEQ ID NOs. 5, 6) are very similar as are VR4 (SEQ ID NOs. 7, 8) and VR5 (SEQ ID NOs. 9, 10), and VR6 (SEQ ID NOs. 11, 12) and VR7 (SEQ ID NOs. 13, 14) (Figure 1). Nonetheless, our results indicate that all of these cDNAs were derived from different genes. First, all cDNAs were sequenced on both strands to rule out sequencing errors. Second, the RNA used for library construction and PCR came from an inbred mouse strain (C57BL/6J), so they cannot be allelic variants. Third, the error rates of reverse transcriptase (or Taq polymerase) cannot account for the extent to which the cDNAs differ. For example, VR4 (SEQ ID NOs. 7, 8) and VR5 (SEQ ID NOs. 9, 10) cDNAs are 99% identical in nucleotide sequence, but the reverse transcriptase used to prepare them has an error rate of only 3.6 x 10-5/bp (Ji, J., et al., Biochemistry, 1992, 31:954-958).

Variant forms of VR mRNA

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Many of the VRs we characterized lacked a segment of the N-terminal domain present in other VRs. Invariably, the missing segment corresponded to a region of the human CSR encoded by a single exon, or pair of exons (Pollak, M., et al., Cell, 1993, 73:1297-1303). We also found several different VR cDNAs that contained a stretch of noncoding sequence at a site corresponding to a CSR exon-intron boundary (e.g. VR15). This suggested that the exon-intron

structure of VR genes resembles that of the CSR gene, and that variant forms of VR mRNAs might be generated by differential RNA splicing.

Variant VR mRNAs could derive either from different genes, or from the same gene by alternative RNA splicing. Consistent with the latter possibility, two pairs of cDNAs that we sequenced VR8 (SEQ ID NOs. 15, 16) and VR9 (SEQ ID NOs. 17, 18), and VR10 (SEQ ID NOs. 19, 20) and VR11 (SEQ ID NOs. 21, 22) were identical in nucleotide sequence, but were missing different segments. However, when we used RT-PCR to amplify VNO mRNA sequences encoding 5 different VRs, we obtained one major PCR product in each case, regardless of whether the RNA used was from male or female mice. In 4 cases, the size of the major product corresponded to a complete VR, even though one of the cDNAs (but not the PCR product) contained an intron (#5). In one case, in which the cDNA lacked one exon (#2), the major PCR product was even smaller, and was found to lack two exons. Although PCR products of a smaller size were also seen in these experiments, they were much less abundant.

These results suggest that different VR forms derive from different genes. Thus many VR genes may be expressed pseudogenes, which either lack one or more exons, or have mutations that prevent proper RNA splicing. We cannot exclude the possibility that some variant VRs are functional, however. For example, some truncated VRs that lack transmembrane domains could conceivably be secreted pheromone-binding proteins.

20 Differential expression of VR genes in VNO neurons

To investigate the tissue distribution of VR gene expression, we conducted Northern blot analyses in which size fractionated polyA⁺ RNAs from different mouse tissues were hybridized to a mix of radiolabeled VR cDNAs. The mixed probe hybridized to VNO RNAs of ~1.9-3.7 kb, with intense hybridization to RNAs of 2.8-3.5 kb. It did not hybridize to RNAs from a variety of other tissues, including olfactory epithelium and brain. This suggested that VR genes may be expressed exclusively in the VNO.

We found two partial cDNAs that were highly related to VR cDNAs in the NCBI dbEST database, one from spleen and the other from 2-cell stage mouse embryos. However, when we hybridized the most highly related VR cDNAs (VR6 and VR7) to spleen sections, only one questionably-labeled cell was seen out of ~1.4 x 10° cells with one VR probe, and none was seen with the other. The EST clones might be DNA contaminants, or be due to the widespread, but low level, misexpression of tissue specific genes (Sarkar, G., et al., *Science*, 1989, 244:331-334);

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nonetheless, we cannot exclude the possibility that VR genes are expressed at a low frequency in some other tissues.

To examine the patterns of expression of different VR genes in the VNO, we conducted in situ hybridization experiments. Labeled segments of the 3' untranslated regions of three VR cDNAs were hybridized separately, or in combination, to sequential sections through the VNO. Probes prepared from G_{ao} and G_{ai2} cDNAs were hybridized to adjacent sections to delineate the G_{ao} + and G_{ai2} + zones of the VNO neuroepithelium.

The G_{so} and G_{si2} probes gave patterns of hybridization similar to those we had previously seen (Berghard, A., et al, *J. Neurosci.*, 1996, 16:909-918). The G_{so} probe hybridized to a wavy stripe of VNO neurons in the basal (lower) region of the VNO neuroepithleium, whereas the G_{si2} probe hybridized to an adjacent stripe of neurons in the apical (upper) part of the neuroepithelium. The waviness of the two zones appears to be caused by the periodic presence of blood vessels near the base of the epithelium (Berghard, A., et al, *J. Neurosci.*, 1996, 16:909-918). Approximately 57% of VNs were labeled by the G_{si2} probe and 43% were labeled by the G_{si2} probe. The single layer of supporting cells located just beneath the epithelial surface was not labeled by either probe.

Each of the VR probes hybridized to a small percentage (2.4-5.7%) of VNs that appeared to be restricted to the basal, G_{ω} + zone of the VNO neuroepithelium. Labeled neurons were scattered throughout the anterior-posterior and dorsal-ventral extent of the G_{ω} + zone. Small clusters of labeled cells were somtimes seen, particularly with the VR2 probe The mixed probe labeled a larger percentage of VNs (10.6%) that was almost equal to the sum of the percentages labeled by its individual components (10.8%). Thus different G_{ω} + neurons must express different VRs.

No differences were seen in the patterns of hybridization obtained using VNOs from male and female mice, and no hybridization was observed in the nasal olfactory epithelium using either the mix of VR probes or a full-length VR cDNA probe (not shown). Subsequent analyses of the size of the VR gene family, and the number of VR genes recognized by the VR in situ hybridization probes, allowed us to estimate the number of VR genes expressed by individual neurons (see below).

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To investigate the size of the VR gene family, we hybridized several different mixed VR gene probes to a mouse genomic library, using high (70°C) or low (55°C) stringency conditions. A probe prepared from the membrane spanning regions (putative exon 6) of several different cDNA clones hybridized to 59 and 98 clones per haploid genome equivalent, at high and low stringency, respectively. To obtain probes that were potentially more diverse, we amplified internal segments of putative exon3 or 6 from genomic DNA by PCR with degenerate primers. At high stringency, these probes hybridized to 60-140 clones per haploid equivalent. These results indicate that there are as many as 140 VR genes in the mouse genome.

The VR probes that we used for in situ hybridization each labeled a small percentage of neurons. To determine how many VR genes each probe recognized, we hybridized probes prepared from the same VR cDNA segments to Southern blots of C57BL/6J mouse genomic DNA which had been digested with Eco RI or Hind III. Each probe hybridized to a small number of restriction fragments. Given the small size of the probes (~350-450 bp), most of these fragments should represent at least one gene, provided that there are no introns in the region probed. Consistent with this assumption, the VR2 (SEQ ID NO. 3) probe hybridized to 7 different restriction fragments, as many as five of which could be accounted for by characterized VR cDNAs that were 91-98% identical to VR2 (SEQ ID NO. 3) in the region probed.

Given the number of genes recognized by each VR probe and the percentage G_{∞} + neurons that hybridized to each, we estimate that each VR gene may be expressed in only ~1.1-1.9% of G_{∞} + VNs. Since there appear to be 60-140 VR genes in the mouse genome, this suggests that each G_{∞} + VNO neuron may express only one, or at most a few, VR genes.

Linkage of chromosomal clusters of VR and OR genes

We previously found that there are clusters of OR genes at multiple chromosomal sites in the mouse genome (Sullivan, S., et al., *Proc. Natl. Acad. Sci.*, 1996, 93:884-888). To investigate the chromosomal locations of VR genes, we used the Jackson Laboratory Backcross DNA Mapping Panel, which allows the mapping of mouse genes using interspecies mouse crosses.

Probes prepared from the 3' untranslated regions of VR2 (SEQ ID NO. 3) or VR4 cDNAs were first hybridized to Southern blots of genomic DNAs from two mouse species, C57BL/6J and Mus spretus, which had been digested with different restriction enzymes. Eco RI digests showed a number of restriction length polymorphisms with both VR probes. The VR probes

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were then hybridized to Eco RI-digested DNAs from a large panel of different backcross mice ((C57BL/6J x M. spretus) x M. spretus).

The patterns of inheritance of the polymorphic fragments recognized by the two VR probes allowed us to assign chromosomal locations to approximately 9 VR genes. Using the VR4 (SEQ ID NO. 7) probe, we could follow the inheritance of 4 polymorphic restriction fragments. All of these cosegregated in the backcrosses, and mapped to the proximal end of chromosome 7 (near *D7Bir5*). Five restriction fragments were followed for the VR2 (SEQ ID NO. 3) probe. Again, all of the restriction fragments cosegregated, allowing us to map the VR2 (SEQ ID NO. 3) fragments to the distal end of chromosome 4 (near *D4Bir1*). Given the resolution of the genetic mapping, the cosegregating fragments can be no more than 3.8 cM from one another. These results indicate that VR genes are located near the ends of at least two different mouse chromosomes. They also indicate that highly related VR genes are clustered at the same chromosomal locus, as previously seen in our studies and others (Ben-Arie et al, *Human Molecular Genetics*, 1994, 3:229-235.).

The VR4 gene subfamily appears to be closely linked to one OR gene locus, (olfR5) (Sullivan, S., et al., Proc. Natl. Acad. Sci., 1996, 93:884-888). Although the VRs and ORs were mapped in different mouse crosses, the synaptotagmin-3 gene (Syt3) was mapped in both crosses, allowing an estimate of their relative positions. The OR locus mapped 15.05 cM proximal to Syt3 while the VR4 gene cluster mapped 14.89 cM proximal to Syt3. (Jackson Laboratory Mouse Genome Informatics), suggesting a close linkage between VR and OR genes at the proximal end of chromosome 7. Our previous studies indicate that multiple OR gene loci arose via a series of duplications of very large chromosomal domains that maintained linkages between OR genes and members of other gene families. These results therefore suggest that VR genes and OR genes might have been linked in a primitive ancestor. They also suggest the possibility that additional clusters of VR genes might be linked to other OR gene loci.

Example 2

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Experimental procedures

Preparation of cDNA Libraries from Isolated VNO Neurons

VNOs were dissected from adult (7- to 8-week-old) male Lewis rats (Sprague-Dawley). Single-cell cDNA synthesis and amplification were performed and checked according to Dulac and Axel (Cell, 1995, 83:195-206). Southern blot analysis of single-cell cDNA was used to

detect expression of tubulin, OMP, Go, and Gi_{2a} (Dulac and Axel, Cell, 1995, 83:195-206). Eighteen cDNAs showed strong hybridization with tubulin and OMP probes, indicating that they originated from mature neurons, and were selected for further study. Cells VN3 and VN13 exhibited high levels of Go expression, whereas VN10 showed presence of Gi_{2a}, indicating the origin of these cells from two distinct regions of the VNO neuroepithelium. VN13 single-cell cDNA library was prepared according to Dulac and Axel (Cell, 1995, 83:195-206).

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Differential Screening of Single-Cell Library

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Plaque-forming units (12 x 10³) from the VN13 library were plated at low density, and duplicate filters (Hybond N⁺, Amersham) were hybridized with probes generated from VN10 and VN13 single-cell cDNAs, following the procedure described in Dulac and Axel, Cell, 1995, 83:195-206. Ten phage plaques were detected that showed a positive signal unique to the VN13 probe. These plaques were purified, and the corresponding phage inserts were amplified by PCR, run on 1.5% agarose gel, blotted onto nylon filter, and hybridized with the VN10, VN3, and VN13 single-cell cDNA probes.

Isolation and Analysis of Full-Length cDNA Clones

A 425 bp clone, Go-VN13A, present at the frequency of 0.1% in the VN13 single-cell cDNA library, was selected and in vivo excised to generate the pBlueScriptSK(-) phagemid. High stringency (65°C) screening of a cDNA library prepared from female rat VNO (Dulac and Axel, Cell, 1995, 83:195-206) with the Go-VN13A cDNA probe led to the isolation of Go-VN13B (SEQ ID NO. 49), presenting 90% sequence homology with Go-VN13A. Phages (7.2 x 10⁵) of the female rat VNO library were further screened with the Go-VN13B (SEQ ID NO. 49) cDNA probe under low stringency conditions: hybridization was carried out at 55°C for 24 hr, and the filters were washed three times at 55°C for 30 min in 0.5x SSC and 0.5% SDS. A total of 75 positive phages were identified and the corresponding inserts were amplified by PCR and analyzed by Southern blot using the Go-VN13B (SEQ ID NO. 49) probe at both high (65°C) and low (55°C) stringency. This led to the identification of 22 cDNA clones with insert sizes longer than 3 kb. Among those, six distinct subfamilies were defined by absence of cross-hybridization under stringent conditions of hybridization and washing. Full-length clones (Go-VN1 to Go-VN6, SEQ ID NOs. 33, 35, 37, 39, 41, 43), each representative of a subfamily, were selected for in vivo excision and sequenced. Go-VN13C (SEQ ID NO. 47) and Go-VN13B (SEQ ID NO. 49) are identical sequences differing by a 150 bp deletion in Go-VN13C (SEQ ID NO. 47). This sequence encodes for NMDQCANCPEYQYANTEKNKCIQKGVIVLSYEDPLGMALALIAFCFSAFTV (SEQ ID NO. 58) in Go-VN13B (SEQ ID NO. 49) and is replaced by an M at position 552 in Go-VN13C (SEQ ID NO. 48).

DNA Sequencing and Sequence Analysis

DNA sequencing was performed using ABI Prism dye terminator cycle ready reaction (Perkin Elmer, Norwalk, CT) according to manufacturer's protocol. Samples were run on an ABI Prism 310 Genetic Analyzer (Perkin Elmer, Norwalk, CT). Sequence homologies were determined using the BLAST system (NIH network service). Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis were obtained with the MacVector sequence analysis software (Oxford Molecular Group).

5 In Situ Hybridization Analysis

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In situ hybridization was performed as described elsewhere (Schaeren-Wiemers, N., et al., *Histochemistry*, 1993, 100:431-440). VNOs were dissected from adult male (8- to 9-week-old), adult female (9- to 11-week-old), and young (1-week-old) rats. Tissues were embedded in Tissue-Tek OCT. Antisense and sense digoxigenin-labeled probes were generated from the full-length cDNAs encoding for Go, Gi_{2x}, Go-VN13B (SEQ ID NO. 49), and Go-VN1 to Go-VN6 (SEQ ID NOs. 33, 35, 37, 39, 41, 43), as well as from the 3' untranslated regions of the Go-VN1 to Go-VN6 clones.

Imaging Processing and Statistical Analysis

Digital photographs were captured with a Leitz DMRB microscope (Leica) coupled to a ProgRes3012 digital camera (Kontron Electronic) and further processed with the Photoshop (Adobe System) and Canvas (Deneba) software for Macintosh. The relative positions of cells exhibiting a positive signal by in situ hybridization were measured along the basal-apical axis using the NIH Image analysis software. The number of cells in hemiconcentric sections of 10% along this axis from the basal (value = 0) to the apical (value = 100) boundaries was determined. Average data for Go-VN1 and Go-VN3 to Go-VN6 were obtained from six to eight VNO sections, corresponding to four individuals analyzed in two independent experiments. For

Go-VN2, 14 VNO sections, corresponding to ten individuals and four independent experiments, were analyzed for each sex.

Southern Blot Analysis of Rat Genomic DNA and Screening of Rat and Human Genomic Libraries

Genomic DNA, prepared from Lewis rat (Sprague-Dawley) liver, was digested with the restriction enzymes EcoRI and BamHI, size fractionated on 0.8% agarose gels, and blotted onto nylon membrane (Sambrook, J., et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989). Membranes were cross-linked under UV light, hybridized overnight at both high (68°C) and low (55°C) stringency in hybridization buffer, and washed as described above. ³²P-labeled probes were generated by random priming, using the following DNA templates: EcoRI-EcoRV, NotI-NsiI, EcoRI-SalI, PstI-NdeI, XbaI-HincII, and EcoRI-NsiI fragments of Go-VN1 to Go-VN6 (SEQ ID NOs. 33, 35, 37, 39, 41, 43), respectively; a full-length (425 bp) insert of Go-VN13A; and a cDNA fragment including the seven transmembrane domains of Go-VN13B (SEQ ID NO. 49). Plaque-forming units (3 x 10⁵) from rat and human genomic libraries (Stratagene, La Jolla, CA) were screened at low stringency (55°C) using a mix of ³²P-labeled probes prepared from fragments of Go-VN1 to Go-VN6 (SEQ ID NOs. 33, 35, 37, 39, 41, 43) encompassing the transmembrane domains 2 to 7.

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Results

The VNO Neuroepithelium Expresses Two Independent Families of Pheromone Receptors

We hypothesized the existence of two distinct families of genes encoding pheromone receptor genes that are selectively colocalized with either the Go protein in the basal half of the vomeronasal neuroepithelium or with the $Gi_{2\alpha}$ protein in the apical region. For simplicity of nomenclature, and with the understanding that the cosegregation of distinct G-protein subunits with independent families of pheromone receptors is consistent but does not demonstrate a functional link, the family of genes encoding putative pheromone receptors that we have previously identified and that colocalize with $Gi_{2\alpha}$ will be named $Gi_{2\alpha}$ -VN, whereas the novel family of receptors coexpressed with Go and described in this study will be named Go-VN. In the absence of information concerning the nature of the Go-VN receptor molecules, we reiterated the cloning strategy that allowed us to identify a family of putative pheromone receptor genes

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expressed by Gi_{2α}+ neurons (Dulac and Axel, Cell, 1995, 83:195-206). This strategy was based on the assumption that individual neurons within the VNO are likely to express only one pheromone receptor gene and that transcripts encoding a given receptor represent between 1% and 0.1% of a single-cell mRNA. Differential screening of cDNA libraries constructed from single-VNO neurons takes advantage of the fact that different cells express different receptors and thus provides an experimental solution to the problem of detecting a specific transcript in a heterogeneous population of neurons. In this attempt, we expected that differential screening of a cDNA library prepared from an isolated Go+, Gi_{2α}- VNO neuron would permit the isolation of a class of pheromone receptor genes distinct from the Gi_{2α}-VN family of receptor genes.

A cDNA library prepared from a Go+ neuron (VN13) was differentially hybridized with ³²P-labeled probes prepared from VN13 and from a second VNO neuron cDNA (VN10). A 425 bp cDNA (Go-VN13A) present at a frequency of 0.1% in the VN13-cDNA library showed selective hybridization with VN13 cell probe. Two cDNAs of longer size, Go-VN13B (SEQ ID NO. 49) and Go-VN13C (SEQ ID NO. 47), were subsequently isolated from a cDNA library prepared from dissected adult VNOs and showed 90% sequence similarity with Go-VN13A. Hybridization to VNO cross-sections with digoxigenin-labeled antisense RNA probe showed that expression of these transcripts is restricted to a small subpopulation of VNO neurons in a location consistent with the region of Go expression of the neuroepithelium. The sequence of Go-VN13B (SEQ ID NO. 49) reveals a partial open reading frame that includes seven hydrophobic stretches of 20 amino acids in length. Go-VN13B (SEQ ID NO. 49) sequence does not share any resemblance with the odorant receptor genes nor with the family of putative pheromone receptor genes previously identified (see below). In addition, hybridization of Go-VN13B DNA probe to genomic DNA identified two discrete bands at high stringency and 13 or more at lower stringency, revealing the existence of a family of closely related genes in the rat genome.

Taken together, these data indicate that we have isolated a novel multigene family encoding seven transmembrane domain receptors and expressed by subsets of VNO neurons from the basal half of the neuroepithelium.

30 Sequences of a New Family of VNO Receptors

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Recombinant phages from a VNO cDNA library were screened at low stringency with the Go-VN13B (SEQ ID NO. 49) DNA probe. Six distinct gene subfamilies were isolated that

showed no cross-hybridization under stringent conditions of hybridization and washing. cDNAs Go-VN1 to Go-VN6, each representative of a subfamily, were fully sequenced (SEQ ID Nos 33, 35, 37, 39, 41 and 43).

In Go-VN1 to Go-VN5 cDNAs (SEQ ID Nos 33, 35, 37, 39 and 41), the first methionine of the open reading frame was tentatively chosen as a start for protein translation, revealing large open reading frames ranging from 548 to 866 amino acids. A frame shift in the Go-VN6 (SEQ ID NO. 44) sequence (amino acid 532; indicated by slash bar in Fig. 3) indicated that this transcript is unable to generate a functional protein.

Deduced Amino Acid Sequences of cDNAs from the Go-VN Family of Pheromone Receptors

The deduced amino acid sequences of eight cDNAs belonging to the Go-VN family of putative pheromone receptors is shown in Figure 3. Predicted position of seven transmembrane domains is also indicated (I-VII). Amino acids common to at least five cDNAs are shaded. Amino acids common to the rat mGluR1 and Ca2+-sensing receptors are indicated by a star.

Hydropathy analysis of the predicted Go-VN proteins with the Kyte-Doolittle algorithm identified a large hydrophilic N-terminal domain that ranges in size from 274 amino acids in Go-VN1 (SEQ ID NO. 34) to 595 in Go-VN4 (SEQ ID NO. 40). This is preceded in cDNAs Go-VN4 (SEQ ID NO. 40), Go-VN7 (SEQ ID NO. 46), and Go-VN13C (SEQ ID NO. 50) by an initial hydrophobic 21 amino acid segment characteristic of eukaryotic signal sequences. A cluster of seven hydrophobic regions representing potential membrane-spanning helices and typical of the G protein-coupled receptor superfamily is followed by a short hydrophilic sequence that indicates a potential intracytoplasmic C-terminal domain. A database search indicated the presence of sequence motifs common to Ca2+-sensing and metabotropic glutamate (mGluR) receptors (Houamed, K., et al., Science, 1991, 252:1318-1321; Masu, M., et al., Nature, 1991, 349:760-765; Brown, E., et al., Nature, 1993, 366:575-580; Pollak, M., et al., Cell, 1993 75:1297-1303). Pairwise sequence alignments reveal 18% to 23% sequence identity between the rat Ca2+-sensing receptor and the most distant (Go-VN3, SEQ ID Nos.37, 38) and the closest (Go-VN1, SEQ ID NOs. 33, 34) Go-VN sequences, respectively. Sequences of rat mGluR1 and Go-VN cDNAs appear more distantly related. Several localized regions showed a more pronounced degree of similarity, including a cysteine-rich sequence just preceding the first transmembrane domain (amino acid 206 to 260 in Go-VN1, SEO ID NO. 34), the predicted

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transmembrane domains 2 to 7 with surrounding cytoplasmic and extracellular loops, and the relative position of 20 cysteines. The N-terminal and first transmembrane domains show little degree of homology. In mGluR and Ca2+-sensing receptors, the second intracellular loop is involved in providing specificity for G-protein coupling (Gomeza, J., et al., J. Biol. Chem., 1996, 271:2199-2205), enabling different classes of mGluR receptors to activate phospholipase C or to inhibit adenylyl cyclase. In Go-VN, this domain is rich in basic residues, as expected for potential G-protein coupling, and shows closer resemblance to the class II and III mGluRs that were shown to couple to Go and Gi subunits. Overall, the six Go-VN sequences share between 42% and 75% sequence identity. Regions of Go-VN proteins downstream of transmembrane domain 2 are nearly identical in all VNO receptor sequences. In contrast, N-terminal extracellular regions and first transmembrane domains are quite divergent.

Anomalies in Go-VN cDNA Sequences: Two unusual features were observed in the sequence of some Go-VN cDNAs. In Go-VN1 (SEQ ID NO. 33) and Go-VN3 (SEQ ID NO. 37) cDNAs, stretches of open reading frame can be found in the 5' extremity of the cDNAs that generate polypeptide sequences of 310 and and 152 amino acids, respectively, which are interrupted by a frameshift in Go-VN1 and by an insertion of 500 nucleic acids in Go-VN3. The prospective receptor protein sequences indicated for Go-VN1 (SEQ ID NO. 33) and Go-VN3 (SEQ ID NO. 37) (Fig. 3) start at the next available methionin and are therefore significantly shorter than those of other receptor cDNAs.

Go-VN7 (SEQ ID NO. 45) and Go-VN13C (SEQ ID NO. 47) cDNAs show a similar deletion of 150 bp located at the exact same position in the sequence. Strikingly, the 150 bp deletion does not alter the open reading frame but generates a gap that encompasses 34 amino acids upstream of the first transmembrane domain and most of the first transmembrane domain itself.

Hydropathy analysis of Go-VN7 (SEQ ID NO. 46) and Go-VN13C (SEQ ID NO. 48) protein sequences detects only a seven to eight amino acid long hydrophobic stretch that might not be long enough to replace the deleted transmembrane domain 1 and allow the appropriate folding of the protein. Except for the 150 bp gap, sequences of Go-VN13B (SEQ ID NO. 50) and Go-VN13C (SEO ID NO. 48) are identical. This raises the question as to whether both transcripts might originate from alternative splicing of the same gene. Alternatively, they might be transcribed from independent genes that evolved from recent duplication and deletion events.

Size f the Go-VN Family of Genes

We investigated the size of the Go-VN family of receptors by hybridizing ³²P-labeled cDNA probes prepared from regions spanning the most divergent N-terminal half of the receptor protein to rat genomic DNA. Individual probes identify two to four discrete bands under stringent conditions of hybridization and washing. Under conditions of reduced stringency, each of the individual probes now generates a unique pattern of 12 to 20 bands, providing a direct illustration of the existence of a very large family of related genes.

A direct estimate of the size of the Go-VN receptor gene family was obtained by low stringency screening of a rat genomic library. PCR amplification on genomic DNA had indicated that receptor genes are devoid of introns in the region encompassing transmembrane domains 2 to 7, enabling us to deduce directly the number of genes present in the rat genome. A mix of ³²P-labeled DNA probes prepared from the six Go-VN cDNA fragments identified 110 positive clones per haploid genome, indicating that the family of Go-VN receptors may consist of 100 genes.

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Expression Pattern of Go-VN Receptors

The pattern of expression of the Go-VN receptor genes was examined by in situ hybridization with digoxigenin-labeled RNA antisense probes. No signal was observed after hybridizing the mix of Go-VN1 to Go-VN6 (SEQ ID NOs. 33, 35, 37, 39, 41 and 43) receptor probes to sections of muscle, testis, brain, or whole head. The adult olfactory epithelium was also consistently negative, although rare positive cells (one to three cells per section) were observed in the olfactory neuroepithelium of E19 rat embryo. In contrast, strong signals were observed when antisense receptor RNA probes were hybridized to VNO neuroepithelium. In adults, each one of the Go-VN probes detects small subsets of VNO sensory neurons. When hybridization and washing were performed at lower temperature, the number of faintly labeled neurons increased, revealing cross- hybridization to more distant receptor genes.

Under high stringency conditions, cDNA clones Go-VN1 to Go-VN6 label 1.9%, 3.6%, 6.1%, 0.4%, 3.5%, and 1.3% of the VNO sensory neurons, respectively. Under the same experimental conditions, the mix of all six Go-VN RNA probes labels 19% of the cells. This number is similar to the sum of labeled neurons detected with the six individual Go-VN probes (17%), indicating that probes representing the six receptor subfamilies recognize distinct populations of VNO sensory neurons. Spatial Distribution of Go-VN Receptor Transcripts

Positive neurons identified with each of the Go-VN probes were randomly distributed along the anteroposterior and dorso-ventral axis of the VNO neuroepithelium. Most RNA probes recognize cells that are preferentially localized in the most basal two-thirds of the neuroepithelium corresponding to the zone of Go expression. However, careful examination of adjacent cross-sections of vomeronasal neuroepithelium labeled with each of the Go-VN probes reveals a well-organized spatial distribution of receptor expression. Different receptors appear preferentially localized in radial zones that define a series of hemiconcentric rings of distinct diameters. This pattern is observed along the entire length of the VNO and is conserved in all animals analyzed. The Go-VN3 (SEQ ID NO. 37) probe, for example, recognizes a subset of neurons that are confined to the most basal third of the VNO neuroepithelium. In contrast, the Go-VN1 (SEQ ID NO. 33), Go-VN4 (SEQ ID NO. 39), and Go-VN5 (SEQ ID NO. 41) RNA probes identify cells restricted to a hemiconcentric zone immediately apical to the area of Go-VN3 expression, whereas Go-VN2 identifies cells apposed to the apical layer of supporting cells. Go-VN6 in turn is found only in sparse cells immediately apposed to the basal membrane. This is best seen in a statistical representation of Go-VN receptor localization collected from VNO sections and multiple animals that shows a striking conservation of these patterns. Thus, transcription of Go-VN cDNAs appears restricted to one of three circumscribed areas of the VNO neuroepithelium in a manner quite reminiscent of the odorant receptor gene expression in four zones of the MOE (Ressler, K., et al., Cell, 1993, 73:597-609; Vassar, R., et al., Cell, 1993, 74:309-318). Although Go-VN3 (SEQ ID NO. 37) and Go-VN6 (SEQ ID NO. 43) transcripts show a clear segregation in the most basal region of the VNO neuroepithelium, the sequence anomalies found in both transcripts leave the functionality of this area of the neuroepithelium as an open question.

25 Sexual Dimorphism in Receptor Distribution and Age-Related Changes

To identify potential sexual dimorphism in Go-VN receptor expression, we systematically hybridized each probe to sections originating from adult male and female rat VNOs. All receptors were equally distributed in males and females with the striking exception of Go-VN2 (SEQ ID NO. 35). In females, Go-VN2 appears expressed in a large and centrally located region comprising one-third of the neuroepithelium. In sharp contrast, the same probe recognizes in males a cohort of cells in the most apical side of the neuroepithelium, closely apposed to the VNO lumen, and most likely intermingled with $Gi_{2\alpha}$ VNO sensory neurons. Such a difference

in the Go-VN2 expression pattern in males and females might result from the expression of the same receptor gene in a different zone of the VNO epithelium or from a differential expression of two distinct but closely related genes of the Go-VN2 subfamily. In females, Go-VN2 generates a very intense hybridization signal to most positive neurons and a fainter staining on a second set of labeled cells. The population of faintly labeled cells was never detected in males, indicating the existence of a female-specific neuronal subpopulation expressing either a lower level of the Go-VN2 transcript or a female-specific receptor significantly different but still cross-hybridizing to the Go-VN2 probe. We followed the emergence of receptor expression and of the VNO zonal organization during development and postnatal stages preceding puberty. Go-VN receptor expression is first detected in the VNO of E14 embryos. No significant difference is observed in the onset of expression of $\text{Gi}_{2\alpha}\text{-VN}$ and Go-VN classes of receptor genes. In agreement with data of Berghard and Buck, 1996 in mouse, segregation of Gi_{2a} and Go expression in the apical and basal areas of VNO neuroepithelium, respectively, is not apparent in the embryo and in 1-week-old animals. In contrast, Gi_{2a}^+ cells appear randomly distributed in large clusters over the whole thickness of the neuroepithelium, intermingled with Go cells. At 4 weeks after birth, however, $Gi_{2\alpha}$ cells appear clearly localized in the apex of the epithelium. Similarly, in situ hybridization experiments with mixes of Go-VN and Gi_{2α}-VN receptor probes on sections of the VNOs dissected from late embryos and 1-week-old animals show that the two cell populations are still intermingled at early postnatal stages. We observed that the zonal distribution of the two families of receptors slowly emerges during sexual 20 maturation to reach the spatial distribution observed in adults. Preliminary data indicate that the sexual dimorphic expression pattern of Go-VN2 is undetectable at 6 weeks after birth. Thus, in contrast to the zones of olfactory receptor gene expression, which are already present in the olfactory epithelium at the earliest stages of receptor gene expression in the embryo (Sullivan, S., et al., Neuron, 1995, 15:779-789), the spatial organization of the VNO neuroepithelium as detected by G-protein and receptor gene expression emerges only in a late postnatal period and reaches its definitive pattern at sexual maturity.

Expression of Go-VN Receptors Is Restricted to Go+ VNO Neurons

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The expression of some of the Go-VN receptors in neurons lining the VNO lumen in an area mainly occupied by $Gi_{2\alpha}$ + cells raises the obvious question as to whether the expression of this family of genes is strictly restricted to Go+ VNO neurons. Single-cell cDNA prepared from

23 individual VNO neurons was analyzed by Southern blots with probes representing the six divergent subfamilies of Go-VN receptors and was PCR amplified with degenerated primers based on conserved motifs between Go-VN receptor sequences. Both approaches confirmed that none of the 19 cell cDNAs prepared from $\text{Gi}_{2\alpha}^+$ neurons contained any sequence of the Go-VN receptor family. In contrast, all four cDNAs generated from $\text{Gi}_{2\alpha}^-$ cells contained a sequence related to the Go-VN receptors. PCR products generated with degenerated primers based on conserved motifs between Go-VN receptor sequences and obtained from the four Go+ cells were subcloned and sequenced. For each single-cell cDNA, the insert sequences from ten independent colonies were found to be identical. This set of data strongly suggests that Go-VN receptor genes are not expressed by $\text{Gi}_{2\alpha}^+$ neurons and constitutes preliminary evidence for the expression of only one Go-VN receptor gene per neuron.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims. All references disclosed herein are incorporated by reference in their entirety.

A Sequence Listing is presented below and is followed by what is claimed.

- 62 -

SEQUENCE LISTING

- (1) GENERAL INFORMATION
- (i) APPLICANT: PRESIDENT AND FELLOWS OF HARVARD COLLEGE
- (ii) TITLE OF THE INVENTION: NOVEL PHEROMONE RECEPTORS
- (iii) NUMBER OF SEQUENCES: 92
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Wolf, Greenfield & Sacks, P.C.
 - (B) STREET: 600 Atlantic Avenue
 - (C) CITY: Boston
 - (D) STATE: MA
 - (E) COUNTRY: U.S.A.
 - (F) ZIP: 02210-2211
- (v) COMPUTER READABLE FORM:
- (A) MEDIUM TYPE: Diskette
- (B) COMPUTER: IBM Compatible(C) OPERATING SYSTEM: DOS
- (D) SOFTWARE: FastSEQ for Windows Version 2.0
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE:
 - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: 60/051,284
 - (B) FILING DATE: 30-JUN-1997
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Plumer, Elizabeth R.
 - (B) REGISTRATION NUMBER: 36,637
 - (C) REFERENCE/DOCKET NUMBER: H0498/7074
- (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: 617-720-3500
 - (B) TELEFAX: 617-720-2441
 - (C) TELEX:
 - (2) INFORMATION FOR SEQ ID NO:1:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3080 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 57...2606
 - (D) OTHER INFORMATION: VR1
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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																-
															Met 1	
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					TTG Leu											155
AAT Asn	AGT Ser 35	GAA Glu	GAT Asp	AGT Ser	GAT Asp	GGA Gly 40	GAT Asp	TTA Leu	CAA Gln	AGG Arg	GAA Glu 45	TGT Cys	CAT His	TTT Phe	TAC Tyr	203
CTT Leu 50	TGG Trp	AAA Lys	ACT Thr	GAT Asp	GAA Glu 55	CCT Pro	ATT Ile	GAA Glu	GAT Asp	AGT Ser 60	TTT Phe	TAT Tyr	TAA Asn	TAT Tyr	GAT Asp 65	251
TTA Leu	AGT Ser	TTT Phe	AGA Arg	ATT Ile 70	GCA Ala	GCA Ala	AGT Ser	GAA Glu	TAT Tyr 75	GAG Glu	TTT Phe	CTT Leu	CTC Leu	GTA Val 80	ATG Met	299
TTT Phe	TTT Phe	GCT Ala	ATC Ile 85	GAT Asp	GAG Glu	ATC Ile	AAC Asn	AGG Arg 90	AAT Asn	CCT Pro	TAT Tyr	CTT Leu	TTA Leu 95	CCC Pro	AAC Asn	347
					TCC Ser											395
AGA Arg	GTT Val 115	ATG Met	GAC Asp	CAA Gln	GCA Ala	TAT Tyr 120	ACA Thr	CAA Gln	ATA Ile	AAT Asn	GGA Gly 125	CAT His	ATG Met	AAT Asn	TTT Phe	443
					TAT Tyr 135											491
					ACT Thr											539
					GGA Gly											587
					CAT His											635
CAT His	GGC Gly 195	ATG Met	GTC Val	TCC Ser	TTG Leu	ATG Met 200	TTT Phe	CAC His	TTT Phe	AGA Arg	TGG Trp 205	ACT Thr	TGG Trp	ATA Ile	GGA Gly	683
					GAT Asp 215											731
					AGG Arg											779
					CAG Gln										GAT Asp.	827

- 64 -

	245	250		255	
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GCT CGG AGA Ala Arg Arg 290	ATC TGG ATC A Ile Trp Ile T 295	CA ACC TCA hr Thr Ser	CAA TGG GAT GT Gln Trp Asp Va 300	C ATC ACA AAT 97 l lle Thr Asn 305	11
AAA AAA GAC Lys Lys Asp	TTC ACC CTT A Phe Thr Leu A 310	sn Leu Phe	CAT GGG ATC ATC His Gly Ile Ilo 315	C ACT TTT GAA 101 e Thr Phe Glu 320	.9
His His Arg	Phe Glu Ile F 325	ro Lys Leu . 330	AAT AAA TTC AT Asn Lys Phe Me	t Gln Thr Met 335	57
AAC ACT GCC Asn Thr Ala 340	AAA TAC CCA G Lys Tyr Pro V	TA GAT ATT al Asp Ile 345	TCT CAT ACT AT Ser His Thr Il 35	e Leu Glu Trp	.5
Asn Tyr Phe 355	Asn Cys Ser I	le Ser Lys . 60	AAC AGC ATT AG Asn Ser Ile Ar 365	g Met His His	;3
ATT ACA TTC Ile Thr Phe 370	AAC AAC ACC T Asn Asn Thr L 375	TG GAA TGG . eu Glu Trp	ACA TCA CTG CA Thr Ser Leu Hi 380	C AAC TAT GAT 121 s Asn Tyr Asp 385	.1
		ly Tyr Asn	TTG TAC AAT GC Leu Tyr Asn Al: 395		;9
			TTT CAA CAA GT Phe Gln Gln Va		17
			ACT GCT TGT CAC Thr Ala Cys Gli 430	n Gln Val Ser	;5
	Lys Thr Arg V		AAC CCT GTT GG Asn Pro Val Gly 445		13
AAC ATG AAG Asn Met Lys 450	CAT AGG GAA A His Arg Glu A 455	AT CAG TGT : sn Gln Cys '	ACA GAG TAT GA Thr Glu Tyr As 460	F ATT TTC ATC 145 p Ile Phe Ile 465	1
		ly Leu Gly	TTA AAA GTG AA Leu Lys Val Lys 475		19
TAT TTA CCT Tyr Leu Pro	TGT TTT CCA C Cys Phe Pro G 485	AG AGA CAA 1 ln Arg Gln 1 490	AAA CTT CAT AT Lys Leu His Il	A TCT GAT GAT 154 e Ser Asp Asp 495	17
			CCT CAG GTT CC Pro Gln Val Pro 51	o Ser Ser Val	15

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TGT Cys	AGT Ser 515	GTG Val	GCA Ala	TGT Cys	ACT Thr	GCT Ala 520	GGA Gly	TTC Phe	AGG Arg	AAA Lys	ATT Ile 525	TAT Tyr	CAA Gln	AAA Lys	GAA Glu	1643
ACA Thr 530	GCA Ala	GAC Asp	TGC Cys	TGC Cys	TTT Phe 535	GAT Asp	TGT Cys	GTT Val	CAG Gln	TGC Cys 540	CCA Pro	GAA Glu	AAT Asn	GAG Glu	ATT Ile 545	1691
TCC Ser	AAC Asn	GAA Glu	ACA Thr	GAT Asp 550	ATG Met	GAA Glu	CAG Gln	TGT Cys	GTG Val 555	AGG Arg	TGT Cys	CCA Pro	GAT Asp	GAT Asp 560	AAG Lys	1739
TAT Tyr	GCC Ala	AAC Asn	ATA Ile 565	GAG Glu	CAA Gln	ACC Thr	CAC His	TGC Cys 570	CTC Leu	TCA Ser	AGA Arg	GCT Ala	GTA Val 575	TCA Ser	TTT Phe	1787
CTG Leu	GCT Ala	TAT Tyr 580	GAA Glu	GAT Asp	TCA Ser	TTG Leu	GGG Gly 585	ATG Met	GCT Ala	CTA Leu	GGC Gly	TGC Cys 590	ATG Met	GCA Ala	CTG Leu	1835
TCC Ser	TTC Phe 595	TCA Ser	GCC Ala	ATC Ile	ACA Thr	ATT Ile 600	CTA Leu	ATC Ile	CTC Leu	GTC Val	ACA Thr 605	TTT Phe	GTG Val	AAG Lys	TAC Tyr	1883
AAA Lys 610	GAT Asp	ACT Thr	CCC Pro	ACT Thr	GTG Val 615	AAG Lys	GCC Ala	AAT Asn	AAC Asn	CGC Arg 620	ATT Ile	CTC Leu	AGC Ser	TAC Tyr	ATC Ile 625	1931
CTG Leu	CTC Leu	ATC Ile	TCT Ser	CTC Leu 630	GTC Val	TTC Phe	TGC Cys	TTT Phe	CTC Leu 635	TGC Cys	TCC Ser	CTG Leu	CTC Leu	TTC Phe 640	ATT Ile	1979
												ACC Thr				2027
												AAA Lys 670				2075
												AGG Arg				2123
												ATT Ile				2171
												TCT Ser				2219
												GTC Val				2267
												GGA Gly 750				2315
												GCT Ala				2363
CCT	GAC	ACA	TTC	AAT	GAA	GCC	AAG	TTC	CTA	ACT	TTC	AGC	ATG	CTG	GTG .	2411

Pro 770	Asp	Thr	Phe	Asn	Glu 775	Ala	Lys	Phe	Leu	Thr 780	Phe	Ser	Met	Leu	Val 785	
														ACC Thr 800		2459
														TCT Ser		2507
														ATT Ile		2555
														TTG Leu		2603
TAT Tyr 850	TGA	AACTT	TC 3	ATGGT	FATG	LA AZ	ATGTT	raga i	GA7	ratt(ZAAC	TTAT	rctt2	ATT (TTCAT	2662
CTT	ATA	AAA C	CAG	ract?	C A	CAT	AATA	AAA	LAAT	AGTA	ATAT	CACAC	AT :	TAT	CTTAC	2722
									-						GCTAC	2782
															TATGAG	2842
															TAAGAA	2902
															CTTTCA AGGTAG	2962 3022
														CGGC		3022

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 850 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Lys Gln Leu Cys Ala Phe Thr Ile Ser Leu Leu Phe Leu Lys Phe 5 10 15 Ser, Leu Ile Leu Cys Cys Leu Thr Glu Pro Ser Cys Phe Trp Arg Ile 20 25 Arg Asn Ser Glu Asp Ser Asp Gly Asp Leu Gln Arg Glu Cys His Phe 40 Tyr Leu Trp Lys Thr Asp Glu Pro Ile Glu Asp Ser Phe Tyr Asn Tyr 55 60 Asp Leu Ser Phe Arg Ile Ala Ala Ser Glu Tyr Glu Phe Leu Leu Val 75 70 Met Phe Phe Ala Ile Asp Glu Ile Asn Arg Asn Pro Tyr Leu Leu Pro 85 90 Asn Ile Thr Leu Met Phe Ser Phe Ile Gly Gly Asn Cys Gln Asp Leu 100 105 110 Leu Arg Val Met Asp Gln Ala Tyr Thr Gln Ile Asn Gly His Met Asn 120 115 125 Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Ala Ile Gly Leu 130 135 140 Thr Gly Pro Ser Trp Lys Thr Ser Leu Lys Leu Ala Met His Ser Ser 155 150 Met Pro Leu Val Phe Phe Gly Pro Phe Asn Pro Asn Leu Arg Asp His.

Asp Arg Leu Pro His Val His Gln Val Ala Pro Lys Asp Thr His Leu Ser His Gly Met Val Ser Leu Met Phe His Phe Arg Trp Thr Trp Ile Gly Leu Val Ile Ser Asp Asp Asp Gln Gly Ile Gln Phe Leu Ser Asp Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr Asp Lys His Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly Glu Met Asn Ser Thr Leu Glu Ala Ser Phe Arg Arg Trp Glu Glu Leu Gly Ala Arg Arg Ile Trp Ile Thr Thr Ser Gln Trp Asp Val Ile Thr Asn Lys Lys Asp Phe Thr Leu Asn Leu Phe His Gly Ile Ile Thr Phe Glu His His Arg Phe Glu Ile Pro Lys Leu Asn Lys Phe Met Gln Thr Met Asn Thr Ala Lys Tyr Pro Val Asp Ile Ser His Thr Ile Leu Glu Trp Asn Tyr Phe Asn Cys Ser Ile Ser Lys Asn Ser Ile Arg Met His His Ile Thr Phe Asn Asn Thr Leu Glu Trp Thr Ser Leu His Asn Tyr Asp Val Ala Met Ser Asp Glu Gly Tyr Asn Leu Tyr Asn Ala Val Tyr Ala Val Ala His Thr Tyr His Glu Tyr Ile Phe Gln Gln Val Glu Ser Gln Lys Lys Ala Lys Pro Lys Arg Tyr Phe Thr Ala Cys Gln Gln Val Ser Ser Leu Met Lys Thr Arg Val Phe Thr Asn Pro Val Gly Glu Leu Val Asn Met Lys His Arg Glu Asn Gln Cys Thr Glu Tyr Asp Ile Phe Ile Ile Trp Asn Phe Pro Gln Gly Leu Gly Leu Lys Val Lys Ile Gly Ser Tyr Leu Pro Cys Phe Pro Gln Arg Gln Lys Leu His Ile Ser Asp Asp Leu Glu Trp Ala Lys Gly Gly Thr Ser Pro Gln Val Pro Ser Ser Val Cys Ser Val Ala Cys Thr Ala Gly Phe Arg Lys Ile Tyr Gln Lys Glu Thr Ala Asp Cys Cys Phe Asp Cys Val Gln Cys Pro Glu Asn Glu Ile Ser Asn Glu Thr Asp Met Glu Gln Cys Val Arg Cys Pro Asp Asp Lys Tyr Ala Asn Ile Glu Gln Thr His Cys Leu Ser Arg Ala Val Ser Phe Leu Ala Tyr Glu Asp Ser Leu Gly Met Ala Leu Gly Cys Met Ala Leu Ser Phe Ser Ala Ile Thr Ile Leu Ile Leu Val Thr Phe Val Lys Tyr Lys Asp Thr Pro Thr Val Lys Ala Asn Asn Arg Ile Leu Ser Tyr Ile Leu Leu Ile Ser Leu Val Phe Cys Phe Leu Cys Ser Leu Leu Phe Ile Gly Pro Pro Asp Gln Val Thr Cys Ile Phe Gln Gln Thr Thr Phe Gly Val Leu Phe Thr Val Ser Val Ser Thr Val Leu Ala Lys Thr Ile Thr Val Val Met Ala Phe Lys Leu Thr Thr Pro Gly Arg Arg Met Arg

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Gly Met Met Met Thr Gly Ala Pro Lys Leu Val Ile Pro Ile Cys Thr 695 700 Leu Ile Gln Leu Val Leu Cys Gly Ile Trp Leu Val Thr Ser Pro Pro 715 705 710 Phe Ile Asp Arg Asp Ile Gln Ser Glu His Gly Lys Ile Val Ile Leu 725 730 Cys Asn Lys Gly Ser Val Ile Ala Phe His Val Val Leu Gly Tyr Leu 740 745 Gly Ser Leu Ala Leu Gly Ser Phe Thr Leu Ala Phe Leu Ala Arg Asn 760 765 Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu 775 780 Val Phe Cys Ser Val Trp Ile Thr Phe Leu Pro Val Tyr His Ser Thr 790 795 785 Arg Gly Arg Val Met Val Val Val Glu Val Phe Ser Ile Leu Ala Ser 815 805 810 Ser Ala Gly Leu Leu Met Cys Ile Phe Val Pro Lys Cys Tyr Val Ile 825 830 820 Leu Ile Arg Pro Asp Ser Asn Phe Ile Lys Asn His Lys Gly Lys Leu 840 845 Leu Tyr 850

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2961 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 86...2509
 - (D) OTHER INFORMATION: VR2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

	•							_								
AGACACATCG GTGCAACTGT GTGTGTGATG TTTTTCTGCA TCAGAAACGG ATTTCACAGC														60		
AGCI	CCAT	CT C	'AGA'	CCTA	AG CZ	AGAC	ATG	AAG	CAG	CTC	TGC	ACT	TTC	ACT	ATT	112
							Met 1	ГУЗ	Gln	Leu	Cys 5	Thr	Phe	Thr	Ile	
TCA	TTG	TTG	TTT	CTG	AAG	TTT	TCT	CTC	ATC	TTG	TGC	TGT	TGG	AGT	GAA	160
Ser	Leu	Leu	Phe	Leu	Lys	Phe	Ser	Leu	Ile	Leu	Сув	Cys	Trp	Ser	Glu	
10					15					20					25	
CCA	AGC	TGC	TTT	TGG	AGG	ATA	AAG	AAG	AGT	GAA	GAT	AAT	GAT	GGA	GAT	208
Pro	Ser	Cys	Phe	Trp	Arg	Ile	Lys	Lys	Ser 35	Glu	Asp	Asn	Asp	Gly	Asp	
*				30					33					40		
TTA	CAA	AGG	GAG	TGT	CAT	TTT	TAC	CTT	TGG	AAA	ACT	GAT	GAA	CCT	ATT	256
Leu	Gln	Arg	Glu	Сув	His	Phe	Tyr	Leu	Trp	Lys	Thr	Asp	Glu	Pro	Ile	
			45	-			-	50	_	_			55			
GAA	GAT	AGT	TTT	TAT	AAT	TAT	GAT	TTA	AGT	TTT	AGA	ATT	GCA	GGA	AGT	304
Glu	Asp		Phe	Tyr	Asn	Tyr		Leu	Ser	Phe	Arg		Ala	Gly	Ser	
		60					65					70				
GAA	TAT	GAG	CTT	CTT	CTG	GTA	ATG	TTT	TTT	GCT	ACT	GAT	GAG	ATC	AAC	352
															Asn	
	75					80					85					

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																-
														ATC Ile		. 400
														TAT Tyr 120		448
														TTA Leu		496
														TCC Ser		544
														CCA Pro		592
														CAG Gln		640
														ATG Met 200		688
														GAT Asp		736
														CAT His		784
														ATA Ile		832
														TCA Ser	GCA Ala 265	880
AAG Lys	GTT Val	GTT Val	ATC Ile	Ile	TAT Tyr	Gly	Asp	Met	Asn	Ser	ACT Thr	CTA Leu	GAA Glu	GCA Ala 280	AGC Ser	928
														ACA Thr		976
														AAT Asn		1024
														CCT Pro	AAA Lys	1072
															GAT Asp 345	1120
ATT	TCT	CAT	ACT	ATT	TTG	GAG	TGG	AAT	TAT	TTT	AAT	TGT	TCA	ATC	TCT	. 1168

																_
·Ile	Ser	His	Thr	11e 350	Leu	Glu	Trp	Asn	Тут 355	Phe	Asn	Сув	Ser	Ile 360	Ser	
	AAC Asn															1216
	ACA Thr															1264
	TTG Leu 395															1312
	CTT															1360
	ACT															1408
	AAC Asn															1456
	ACA Thr															1504
	TTA Leu 475															1552
	CAA Gln															1600
	GTG Val															1648
	TTA Leu															1696
ТАТ Туг	GAA Glu	GAT Asp 540	CCA Pro	TTG Leu	GGG Gly	ATG Met	GCT Ala 545	CTA Leu	GGC Gly	TGC Cys	ATG Met	GCA Ala 550	CTG Leu	TCC Ser	TTC Phe	1744
	GCC Ala 555															1792
	CCC															1840
	TCT															1888
	GAC Asp														TTG Leu .	1936

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			605					610					615			
														GTG Val		1984
ATG Met	GCT Ala 635	TTC Phe	AAG Lys	CTC Leu	ACT Thr	ACT Thr 640	CCA Pro	GGA Gly	AGA Arg	AGG Arg	ATG Met 645	AGA Arg	GGG Gly	ATG Met	ATG Met	2032
ATG Met 650	ACA Thr	GGG Gly	GCA Ala	CCT Pro	AAG Lys 655	TTG Leu	GTC Val	ATT Ile	CCC Pro	ATT Ile 660	TGT Cys	ACC Thr	CTG Leu	ATC Ile	CAA Gln 665	2080
														ATT Ile 680		2128
							Gly							AAT Asn		2176
GGC Gly	TCT Ser	GTC Val 700	GTT Val	GCC Ala	TTC Phe	CAC His	GTC Val 705	GTC Val	CTG Leu	GGA Gly	TAC Tyr	TTG Leu 710	GGC Gly	TCC Ser	TTG Leu	2224
														CCT Pro		2272
ACA Thr 730	TTC Phe	AAT Asn	GAA Glu	GCC Ala	AAG Lys 735	TTC Phe	CTA Leu	ACT Thr	TTC Phe	AGC Ser 740	ATG Met	CTG Leu	GTG Val	TTC Phe	TGC Cys 745	2320
														GGG Gly 760		2368
														GCA Ala		2416
														ATT Ile		2464
														TAT Tyr	TGAAA	2514
AGCA AGCA GATO CTGT CATA TACT	AGTAC AAAC TGTC CTTT ACAC TCC	TT CATE ATER ATER ATER ATER ATER ATER ATER A	CATCA NATA: PTTG: NCAGO SGACA	ATATA TGTT(TGTT) CGCCA ATGAA TGCC	AA AA GA GA TA AC AC CT AG CC	AAATA AACTO SCCAT CTAO CAGTA	AAAG: EGGA: FGTA(EGCA: AATC) FATT(TAAT TTT TTT TGCT AAC	PATA(PCAAT PATTA PGTC(PATTA)	CAGA TTGA AATG CTTG CTCC	GGAZ ATTZ AGTZ ACTZ	ATACT ATGGO AACAT FATAL FGCT	TTA (CTA (CTA (CTA (CTA (CTA (CTA (CTA (CAAA(CCAA! GGTT! AAGG(ATGG!	ARTAAA CTGGAC FATTTT ACCCTA GTACTG AGTTCT AAATAA	2574 2634 2694 2754 2814 2874 2934 2961

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 808 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Lys Gln Leu Cys Thr Phe Thr Ile Ser Leu Leu Phe Leu Lys Phe Ser Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser Cys Phe Trp Arg Ile Lys Lys Ser Glu Asp Asn Asp Gly Asp Leu Gln Arg Glu Cys His Phe Tyr Leu Trp Lys Thr Asp Glu Pro Ile Glu Asp Ser Phe Tyr Asn Tyr Asp Leu Ser Phe Arg Ile Ala Gly Ser Glu Tyr Glu Leu Leu Leu Val Met Phe Phe Ala Thr Asp Glu Ile Asn Lys Asn Pro Tyr Leu Leu Pro Asn Met Ser Leu Met Phe Ser Ile Ile Gly Gly Asn Cys His Asp Leu Leu Arg Ser Leu Asp Gln Glu Tyr Ala Gln Ile Asp Gly His Met Asn Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Ala Thr Gly Leu Thr Gly Pro Ser Trp Lys Thr Ser Leu Lys Leu Ala Met His Ser Ser Met Pro Leu Val Phe Phe Gly Pro Phe Asn Pro Asn Leu Arg Asp His Asp Arg Leu Pro His Val His Gln Val Ala Pro Lys Asp Thr His Leu Ser His Gly Met Val Ser Leu Met Phe His Phe Arg Trp Thr Trp Ile Gly Leu Val Ile Ser Asp Asp Gln Gly Ile Gln Phe Leu Ser Asp Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr Asp Thr Gln Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly Asp Met Asn Ser Thr Leu Glu Ala Ser Phe Arg Arg Trp Glu Glu Leu Gly Ala Arg Arg Ile Trp Ile Thr Thr Thr Gln Trp Asp Val Ile Thr Asn Lys Lys Asp Phe Thr Leu Asn Leu Phe His Gly Thr Ile Thr Phe Ala His His Lys Asp Glu Ile Pro Lys Phe Arg Asn Phe Met Gln Thr Lys Lys Thr Ala Lys Tyr Leu Val Asp Ile Ser His Thr Ile Leu Glu Trp Asn Tyr Phe Asn Cys Ser Ile Ser Lys Asn Ser Ser Lys Met Gly His Phe Thr Phe Asn Asn Thr Leu Gln Trp Thr Ala Leu His Asn Tyr Asp Met Ala Leu Ser Asp Glu Gly Tyr Asn Leu Tyr Asn Ala Val Tyr Ala Val Ala His Thr Tyr His Glu Tyr Ile Leu Gln Gln Val Glu Ser Gln Lys Lys Ala Lys Pro Lys Arg Tyr Phe Thr Ala Cys Gln Gln Val Ser Ser Leu Met Lys Thr Arg Val Phe Met Asn Pro Val Gly Glu Leu Val Asn Met Lys His Arg Glu Asn Gln Cys Thr Glu Tyr Asp Ile Phe

Ile Ile Trp Asn Phe Pro Gln Gly Leu Gly Leu Lys Val Lys Val Gly 470 475 Ser Tyr Leu Pro Cys Phe Pro Lys Ser Gln Gln Leu His Ile Ala Asp 485 490 Asp Leu Glu Trp Ala Met Gly Gly Thr Ser Val Asp Met Glu Gln Cys 500 505 510 Val Arg Cys Pro Asp Asn Lys Tyr Ala Asn Leu Glu Gln Thr His Cys 520 515 525 Leu Gln Arg Thr Val Ser Phe Leu Ala Tyr Glu Asp Pro Leu Gly Met 535 540 Ala Leu Gly Cys Met Ala Leu Ser Phe Ser Ala Ile Thr Ile Leu Val 550 555 Leu Val Thr Phe Val Lys Tyr Lys Asp Thr Pro Ile Val Lys Ala Asn 565 570 575 Asn Arg Ile Leu Ser Tyr Ile Leu Leu Ile Ser Leu Val Phe Cys Phe 585 580 590 Leu Cys Ser Leu Leu Phe Ile Gly His Pro Asp Gln Val Thr Cys Ile 595 600 605 Leu Gln Gln Thr Thr Phe Gly Val Leu Phe Thr Val Ser Val Ser Thr 615 620 Val Leu Ala Lys Thr Ile Thr Val Val Met Ala Phe Lys Leu Thr Thr 630 635 Pro Gly Arg Arg Met Arg Gly Met Met Met Thr Gly Ala Pro Lys Leu 645 650 Val Ile Pro Ile Cys Thr Leu Ile Gln Leu Val Leu Cys Gly Ile Trp 665 660 670 Leu Val Thr Ser Pro Pro Phe Ile Asp Arg Asp Ile Gln Ser Glu His 680 675 685 Gly Lys Ile Val Ile Leu Cys Asn Lys Gly Ser Val Val Ala Phe His 690 695 700 Val Val Leu Gly Tyr Leu Gly Ser Leu Ala Leu Gly Ser Phe Thr Leu 710 715 Ala Phe Leu Ala Arg Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe 725 730 735 Leu Thr Phe Ser Met Leu Val Phe Cys Ser Val Trp Ile Thr Phe Leu 740 745 750 Pro Val Tyr His Ser Thr Arg Gly Lys Val Met Val Val Val Glu Val 765 755 760 Phe Ser Ile Leu Ala Ser Ser Ala Gly Leu Leu Met Cys Ile Phe Val 775 770 780 Pro Lys Cys Tyr Val Ile Leu Ile Arg Pro Asp Ser Asn Phe Ile Gln 790 795 Asn His Lys Gly Lys Leu Leu Tyr 805

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2907 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 1...2409
 - (D) OTHER INFORMATION: VR3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CAT TTT TAC CTT GGG GCA GTT GAT AAA CCA ATT GAA GAT AAT TTT TAT His Phe Tyr Leu Gly Ala Val Asp Lys Pro Ile Glu Asp Asn Phe Tyr .

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											-
1			5			10			15		
			AAG Lys								96
			TTT Phe								144
			ACT Thr								192
			GGT Gly								240
			TAA Asn 85								288
		 	CCA Pro	 			 				336
			CTG Leu								384
			CTG Leu								432
			GGC Gly								480
			GTC Val 165								528
			GAA Glu								576
			CCA Pro								624
	_	 _	CAA Gln								672
			AAC Asn							_	720
			CGG Arg 245								768
			AAA Lys								816

																•
					AGA Arg											864
					GCC Ala											912
					TTT Phe 310											960
					TTC Phe				_							1008
					ATG Met											1056
					CAC His											1104
					GCA Ala											1152
					ATG Met 390											1200
					AAG Lys											1248
					AAC Asn											1296
					CCT Pro										ATA Ile	1344
Ser		Asp		Glu	TGG Trp	Ala	Met			Thr						1392
					GCA Ala 470										CAG Gln 480	1440
					TGC Cys											1488
					ACA Thr											1536
					ATA Ile											1584
TCA	TTT	CTG	GCT	TAT	GAA	GAT	CCA	TTG	GGG	ATA	GCT	CTA	GGC	TGC	ATA ·	1632

Ser	Phe	Len	Δ1 =	ጥሙ	G) ··	Ac-	Dro	Len	Glv	Tla	21 =	T.e.u	Glv	Cyre	Tle	
361	530	neu	A.a	TÄT	GLU	535	FIO	nen	GLY	116	540	Leu	GLY	Cys	115	
	CTG Leu															1680
	TAC Tyr															1728
TAC Tyr	ATC Ile	CTG Leu	CTC Leu 580	ATC Ile	TCT Ser	CTA Leu	GTC Val	TTC Phe 585	TGC Cys	TTT Phe	CTC Leu	TGC Cys	TCC Ser 590	CTG Leu	CTC Leu	1776
	ATT Ile															1824
	GGA Gly 610															1872
	ACT Thr															1920
	GAG Glu															1968
	CTA Leu															2016
	TTT Phe															2064
	TGC Cys 690															2112
	GGC Gly															2160
	CTT Leu															2208
	GTG Val															2256
	AGG Arg		Lys													2304
TCT Ser	AGT Ser 770	GCA Ala	GGG Gly	TTG Leu	CTA Leu	ATG Met 775	Cys	ATC Ile	TTT Phe	GTC Val	CCA Pro 780	Lys	тст Сув	TAT Tyr	GTT Val	2352
															AAA Lys .	2400

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785 790 795 800

TTT CGT TAT TGAAATATTC ATACTATGAA AATGTTAGAT TATACTCAAC ATATTTTTC 2458 Phe Arg Tyr

TTTGTCTTAA CAAAAGTAGT ACTTAATCTT ATAAAAATTT AAATAATATA CAAATTTGAA 2518
CTTACAAACA GGACAGAACT GTCTATTGTA ATACCAATTA CAAAACTTTG GTGAAAAATG 2578
GTCTCATTCA TAAGGACACA ATTCTGAAGA TATTGAGAAC CAGGAATCTC AACTGCGGAA 2638
ACGCTACCAT CATCCTGACC TGTGGTTTTG TGTGTAAAGC ATGAACTTAA TTAATGATTA 2698
ATATAAAGGTG ACCATACTGA CTGTGAACAC TACCATCTCT GGGCAAGTTG TTCTTGTAGT 2758
TGTAAGAAAA AGCTCTGAAG ACAACATGGA AGTAAAGCCA GTAATCACCA TTATCCCTCA 2818
TGCTTTCATG GAGTGGCTGC ATCCAATTTC ATGCCTTGGC TTCATTCAAT ATACTGTGAC 2907

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 803 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

His Phe Tyr Leu Gly Ala Val Asp Lys Pro Ile Glu Asp Asn Phe Tyr 10 Asn Ser Leu Leu Lys Phe Arg Ile Ala Ala Ser Glu Tyr Glu Phe Leu 20 25 Leu Val Met Phe Phe Ala Thr Asp Glu Ile Asn Lys Asn Pro Tyr Leu 40 Leu Pro Asn Ile Thr Leu Met Phe Ser Ile Ile Gly Gly Asn Cys His 55 Asp Leu Leu Arg Gly Leu Asp Gln Ala Tyr Thr Gln Ile Asn Gly His 70 75 Met Asn Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Ala Ile 90 Gly Leu Thr Gly Pro Ser Trp Lys Thr Ser Leu Asn Leu Ala Met His 105 Ser Ser Met Pro Leu Val Phe Phe Gly Ser Phe Asn Pro Asn Leu His 120 125 Asp His Asp Arg Leu His His Val His Gln Val Ala Thr Lys Asp Thr 135 140 His Leu Ser His Gly Ile Val Ser Leu Met Phe His Phe Arg Trp Thr 150 155 Trp Ile Gly Leu Val Ile Ser Asp Asp Asp Lys Gly Ile Gln Phe Leu 170 165 Ser Asp Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe 180 185 Val Asn Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr 195 200 205 Ile Tyr Asp Lys Gln Ile Met Thr Ser Leu Ala Lys Val Val Ile Ile 210 215 220 Tyr Gly Glu Met Asn Ser Thr Leu Glu Val Ser Phe Arg Arg Trp Glu 230 235 240 Asn Leu Gly Ala Arg Arg Ile Trp Ile Thr Thr Ser Gln Trp Asp Val 245 250 255 Ile Thr Asn Lys Lys Glu Phe Thr Leu Asn Leu Phe His Gly Thr Ile 265 Thr Phe Ala His Arg Arg Phe Glu Ile Pro Lys Phe Lys Lys Phe Met 280 Gln Thr Met Asn Thr Ala Lys Tyr Pro Val Asp Ile Ser His Thr Ile .

	200					205					200				
	290 Glu	Trp	Asn	Tyr		295 Asn	Cys	Ser	Ile		300 Lys	Asn	Ser	Ser	
305 Met	Asp	His	Ile	Thr	310 Phe	Asn	Asn	Thr	Leu	315 Glu	Trp	Thr	Ala	Leu	320 His
Asn	Tyr	Asp	Met	325 Val	Met	Ser	Asp	Glu	330 Gly	Tyr	Asn	Leu	Tyr	335 Asn	Ala
	-		340					345					350	Gln	
	_	355					360					365			
	370		_	_		375		_	_		380			Cys	
Gln 385	Val	Ser	Ser	Leu	Met 390	Lys	Thr	Arg	Val	Phe 395	Thr	Asn	Pro	Val	Gly 400
Glu	Leu	Val	Asn	Met 405	Lys	His	Arg	Glu	Asn 410	Gln	Cys	Thr	Glu	Tyr 415	Asp
Ile	Phe	Leu	Ile 420	Trp	Asn	Phe	Pro	Gln 425	Gly	Leu	Gly	Leu	Lys 430	Val	Lys
Ile	Gly	Ser		Leu	Pro	Суз	Phe		Gln	Arg	Gln	Glu 445		His	Ile
Ser	Asp		Leu	Glu	Trp	Ala 455		Gly	Gly	Thr	Ser 460		Val	Pro	Ser
Ser 465		Cys	Ser	Val	Ala 470		Thr	Ala	Gly	Phe 475		Lys	Ile	His	Gln 480
	Glu	Thr	Ala	Asp		Сув	Phe	Asp	Cys 490		Gln	Сув	Pro	Glu 495	
Glu	Val	Ser	Asn 500		Thr	Asp	Met	Glu 505		Сув	Val	Lys	Cys 510	Pro	Tyr
Asp	Lys	Tyr 515		Asn	Ile	Glu	Lys 520		His	Сув	Leu	Ser 525		Ala	Val
Ser	Phe 530	-	Ala	Tyr	Glu	Asp 535		Leu	Gly	Ile	Ala 540		Gly	Cys	Ile
Ala 545	-	Ser	Phe	Ser	Ala 550		Thr	Ile	Leu	Val 555		Ile	Thr	Phe	Leu 560
Lys	Tyr	Lys	Asp	Thr 565		Ile	Val	Lys	Ala 570	Asn	Asn	Arg	Ile	Leu 575	Ser
Tyr	Ile	Leu	Leu 580	Ile	Ser	Leu	Val	Phe 585	Cys	Phe	Leu	CAa	Ser 590	Leu	Leu
Phe	Ile	Gly 595	His	Pro	Asn	Gln	Val 600	Ser	Cys	Val	Leu	Gln 605	Gln	Thr	Thr
Phe	Gly 610	Val	Phe	Phe	Thr	Val 615	Ser	Val	Ser	Thr	Val 620	Leu	Ala	Lys	Thr
Ile 625	Thr	Val	Val	Met	Ala 630	Phe	Lys	Leu	Thr	Thr 635	Pro	Gly	Arg	Arg	Met 640
	Glu	Met	Leu	Val 645		Gly	Ala	Pro	Lys 650		Val	Ile	Pro	Ile 655	
Thr	Leu	Ile			Val	Leu	Cys	Gly 665		Trp	Leu	Ile	Thr 670	Ser	Pro
Pro	Phe		660 Asp	Arg	Asp	Ile		Ser	Glu	His	Gly			Val	Ile
Leu	_	675 Asn	Lys	Gly	Ser				Phe	His		685 Val	Leu	Gly	Tyr
	Gly	Ser	Leu	Ala		•		Phe	Thr		700 Ala	Phe	Leu	Ala	_
705 Asn	Leu	Pro	Asp		710 Phe		Glu	Ala	_		Leu	Thr	Phe	Ser	720 Met
Leu	Val	Phe		725 Ser	Val	Trp	Ile				Pro	Val		735 His	Ser
Thr	Arg			Val	Met	Val				Val	Phe		750 Ile	Leu	Ala
Ser		755 Ala		Leu	Leu				Phe	Val			Cys	Tyr	Val
	770 Leu	Val	Arg	Pro				Phe	Ile				ГХв	Asp	
785 Phe	Arg	Tyr			790					795					800

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(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 3625 base pairs
 (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA (ix) FEATURE:
- - (A) NAME/KEY: Coding Sequence (B) LOCATION: 117...2672

 - (D) OTHER INFORMATION: VR4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TGAATATGCA ATAAACCTCA CATTTGCACA AAGAAATAAA AGCTGGTAGA AATCTGATGT GCTGATATGC ATGGCACTTC ACAATCCGCA CTGCCCAGGT TTAAGGCAGG AAAAAG ATC Met 1	119
TTC ATT TTC ATG GGA GTC TTC TTC CTA CTT AAT ATT ACA CTT CTC ATG Phe Ile Phe Met Gly Val Phe Phe Leu Leu Asn Ile Thr Leu Leu Met 5 10 15	167
GCC AAT TTC ATT GAT CCC AGG TGC TTT TGG AGA ATA AAT TTG GAT GAA Ala Asn Phe Ile Asp Pro Arg Cys Phe Trp Arg Ile Asn Leu Asp Glu 20 25 30	215
ATA ACG GAT GAA TAT TTG GGA TTA TCT TGT GCT TTC ATC CTG GCA GCT Ile Thr Asp Glu Tyr Leu Gly Leu Ser Cys Ala Phe Ile Leu Ala Ala 35 40 45	263
GTT CAG ACA CCC ATT GAA AAA GAT TAT TTC AAC ACG ACT CTT AAT TTT Val Gln Thr Pro Ile Glu Lys Asp Tyr Phe Asn Thr Thr Leu Asn Phe 50 55 60 65	311
CTA AAA ACT ACT AAA AAC CAC AAA TAT GCT TTG GCA TTG GTG TTT GCA Leu Lys Thr Thr Lys Asn His Lys Tyr Ala Leu Ala Leu Val Phe Ala 70 75 80	359
ATG GAT GAA ATC AAC AGA TAT CCT GAT CTT TTA CCA AAT ATG TCT TTG Met Asp Glu Ile Asn Arg Tyr Pro Asp Leu Leu Pro Asn Met Ser Leu 85 90 95	407
ATT ATC AGA TAC TCT TTG GGC CAT TGT GAT GGA AAA ACT GTA ACA CCT Ile Ile Arg Tyr Ser Leu Gly His Cys Asp Gly Lys Thr Val Thr Pro 100 105 110	455
ACA CCA TAT TTA TTT CAT AGA AAA AAG CAA AGC CCT ATT CCT AAT TAT Thr Pro Tyr Leu Phe His Arg Lys Lys Gln Ser Pro Ile Pro Asn Tyr 115 120 125	503
TTC TGT AAT GAA GAG AGT ATG TGT TCA TTT CTG CTT TCA GGA CCC AAT Phe Cys Asn Glu Glu Ser Met Cys Ser Phe Leu Leu Ser Gly Pro Asn 130 145	551
TGG GAT GAA TCT TTA AGT TTC TGG AAG TAC CTG GAC AGC TTC TTA TCT TTP Asp Glu Ser Leu Ser Phe Trp Lys Tyr Leu Asp Ser Phe Leu Ser 150 155 160	599
CCA CGT ATC CTT CAG CTT TCC TAT GGA TCT TTC AGT TCC ATC TTC AGT Pro. Arg Ile Leu Gln Leu Ser Tyr Gly Ser Phe Ser Ser Ile Phe Ser .	647

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165	170	175
	Tyr Gln Met Ala	CCA AAA GAC ACA 695 Pro Lys Asp Thr 190
		TTG AAA TGG AAT 743 Leu Lys Trp Asn
		AAC CAA TTT CTT 791 Asn Gln Phe Leu 225
		TGC TTT GCC TTT 839 Cys Phe Ala Phe 240
		CAA AAA ACT GAA 887 Gln Lys Thr Glu 255
	Ser Leu Thr Asn	GTT ATT ATC ATT 935 Val Ile Ile Ile 270
		AGA ATG TGG GAA 983 Arg Met Trp Glu
		CAA TTG AAT TTC 1031 Gln Leu Asn Phe 305
		TAT GGA TCA CTT 1079 Tyr Gly Ser Leu 320
		AAA AAT TTT GTA 1127 Lys Asn Phe Val 335
	Thr Asp Leu Cys	CTA GTA ATG CCA 1175 Leu Val Met Pro 350
		AAT TGT AAA ATA 1223 Asn Cys Lys Ile
		CTA ATG GAA GAG 1271 Leu Met Glu Glu 385
		ATA TAT AAT GCT 1319 Ile Tyr Asn Ala 400
		CTG CAA CAG GCT 1367 Leu Gln Gln Ala 415
	Lys Gly Ala Ser	TCT CAC TGC TTG 1415 Ser His Cys Leu 430

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					CTA Leu											1463
					AAG Lys 455											1511
					AAT Asn											1559
					CCA Pro											1607
TAC Tyr	GTA Val	GAC Asp 500	ATG Met	ATT Ile	GAG Glu	TTG Leu	GCC Ala 505	ACA Thr	GGA Gly	AGA Arg	AGA Arg	AAG Lys 510	ATG Met	CCA Pro	TCC Ser	1655
					GAT Asp											1703
					TGC Cys 535											1751
					ACA Thr											1799
					ACA Thr											1847
					GAA Glu											1895
					GCA Ala											1943
		His	Asp	Thr	CCT Pro 615	Ile	Val	Lys	Ala	Asn	Asn	Arg	Ser	Leu		1991
					TCA Ser											2039
					AAC Asn											2087
					ACT Thr											2135
					GCT Ala											2183
AGA	TAC	TTC	CTT	GTA	TCA	GGG	ACA	CTA	AAC	TAC	ATT	ATT	CCT	ATA	TGT.	2231

TCC CTA CTC CAA TGT GTT CTG TGT GCA ATC TGG CTA GCA GTC TCT CCT Ser Leu Leu Gln Cys Val Leu Cys Ala Ile Trp Leu Ala Val Ser Pro 710 715 720	2279
CCC TTT GTT GAT ATT GAT GAA CAC TCT CAG CAT GGC CAC ATC ATT Pro Phe Val Asp Ile Asp Glu His Ser Gln His Gly His Ile Ile 125 730 735	2327
GTG TGC AAC AAG GGC TCA GTT ACT GCA TTC TAC TGT GTC CTT GGA TAC Val Cys Asn Lys Gly Ser Val Thr Ala Phe Tyr Cys Val Leu Gly Tyr 740 745 750	2375
TTG GCC TGC CTG GCA CTG GGA AGC TTC ACT TTG GCT TTC TTG GCC AAG Leu Ala Cys Leu Ala Leu Gly Ser Phe Thr Leu Ala Phe Leu Ala Lys 755 760 765	2423
AAT CTG CCT GAT GCA TTC AAT GAA GCC AAG TTC TTG ACC TTC AGC ATG Asn Leu Pro Asp Ala Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met 770 785 780 785	2471
CTA GTG TTC TGC AGT GTC TGG GTC ACC TTC CTC CCT GTG TAC CAT AGC Leu Val Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr His Ser 790 795 800	2519
ACA AAG GGC AAA CAC ATG GTT GCT GTG GAG ATC TTC TCT ATC TTG GCA Thr Lys Gly Lys His Met Val Ala Val Glu Ile Phe Ser Ile Leu Ala 805 810 815	2567
TCC AGT GCA GGG ATG CTT GGA TGT ATT TTT GTA CCC AAG ATT TAT ATC Ser Ser Ala Gly Met Leu Gly Cys Ile Phe Val Pro Lys Ile Tyr Ile 820 825 830	2615
ATT TTA ATG AGA CCA GAG AGA AAT TCT ACC CAA AAG ATC AGA GAA AAA Ile Leu Met Arg Pro Glu Arg Asn Ser Thr Gln Lys Ile Arg Glu Lys 835 840 845	2663
TCA TAT TTT TGAACAAATA TTTAGGAATT CTGTCAAATG TAAAGTTGGT ACATAACCA 2 Ser Tyr Phe 850	2721
CCAAATATTG GGTTATAGTG CATGTGTCTA GTTTTAGAAT CACTCTCACT GGTTGCTCTA GTGATAAAAG GAAGTATCAT ATCTACTGAA CTTCCGTACA GTGTCCATAA AATCTTGCAC TCATTCACTT TCTTCATTTT CTCTCAGAGA ACTAAACTCT CTAATTATTA CAATTTTATT CTTCGTTTTG AATTTCATGG AGATTGCCCT CTGGTAACTT CCAAAAAAAC GTTGATAAGG CAGTTTAATC CACCACTTTG TGTAGAAAAA ATGAGATCTA GGACAGACAG GGTTACACAT AAGAACCATC TACCAAATCA AATAATCAAT GAGAAACACA GACTAACTAA ATAATCAGCA AAGTTGAAAT CAGAACTTAT TTTCTGATTT CCAGAAGAG CACCACAGA AGAAAATACT GACTTTTTTT TCTTCTGTT CTTCAAGCTA CTGGCCAATA ATCAGAAGC CAGGATTCT GTGGCTGAAT TGGGAATATT TGGAAGAAGC TGAGGAGGA GGTGACCAG ATTCTCAACA AACCTGGACA AGCAAGATCT CTCAGACACT GAGCCTCTAA CCAGAGATCA TACACAAGCT GATGTGAAGC CCCCAACAAA TATGCACCAT AAGACTGCCT GGTCAGCAC ATTCTCAACA CACCCTAAC CCCAACAAAA TATGCACCAT AAGACTGCCT GGTCTAGCAT CAGTGGGGA CACACCTAAC CCCAGAGAGA CTTAAGTCCC CAGGGATTGG GAAGTGCTGG GCATTGGGGA CACACCAGGA GGGGGATAAC TACTAGATTG TAACAAAAAT ATTGAGTAAT AATAAATTAA	2781 2841 2901 2961 3021 3081 3141 3201 3321 3321 3341 3501 3561 3621

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 852 amino acids(B) TYPE: amino acid

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- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Phe Ile Phe Met Gly Val Phe Phe Leu Leu Asn Ile Thr Leu Leu Met Ala Asn Phe Ile Asp Pro Arg Cys Phe Trp Arg Ile Asn Leu Asp .25 Glu Ile Thr Asp Glu Tyr Leu Gly Leu Ser Cys Ala Phe Ile Leu Ala Ala Val Gln Thr Pro Ile Glu Lys Asp Tyr Phe Asn Thr Thr Leu Asn Phe Leu Lys Thr Thr Lys Asn His Lys Tyr Ala Leu Ala Leu Val Phe Ala Met Asp Glu Ile Asn Arg Tyr Pro Asp Leu Leu Pro Asn Met Ser Leu Ile Ile Arg Tyr Ser Leu Gly His Cys Asp Gly Lys Thr Val Thr Pro Thr Pro Tyr Leu Phe His Arg Lys Lys Gln Ser Pro Ile Pro Asn Tyr Phe Cys Asn Glu Glu Ser Met Cys Ser Phe Leu Leu Ser Gly Pro Asn Trp Asp Glu Ser Leu Ser Phe Trp Lys Tyr Leu Asp Ser Phe Leu Ser Pro Arg Ile Leu Gln Leu Ser Tyr Gly Ser Phe Ser Ser Ile Phe Ser Asp Asp Glu Gln Tyr Pro Tyr Leu Tyr Gln Met Ala Pro Lys Asp Thr Ser Leu Ala Leu Ala Met Val Ser Phe Ile Leu Tyr Leu Lys Trp Asn Trp Ile Gly Leu Val Ile Pro Asp Asp Asp Gln Gly Asn Gln Phe Leu Leu Glu Leu Lys Lys Gln Ser Glu Asn Lys Glu Ile Cys Phe Ala Phe Val Lys Met Ile Ser Val Asp Glu Val Ser Phe Pro Gln Lys Thr Glu Ile Asn Tyr Lys Gln Ile Val Lys Ser Leu Thr Asn Val Ile Ile Ile Tyr Gly Glu Thr Tyr Asn Phe Ile Asp Leu Ile Phe Arg Met Trp Glu Pro Pro Ile Leu Gln Arg Ile Trp Ile Thr Thr Lys Gln Leu Asn Phe Pro Thr Ser Lys Thr Asp Ile Ser His Asp Thr Phe Tyr Gly Ser Leu Thr Phe Leu Pro His His Gly Glu Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Trp Phe His Leu Arg Asn Thr Asp Leu Cys Leu Val Met Pro Glu Trp Lys Tyr Ile Asn Ser Glu Asp Ser Ala Ser Asn Cys Lys Ile Leu Lys Asn Ser Ser Ser Asp Ala Ser Phe Asp Trp Leu Met Glu Glu Lys Leu Asp Met Ala Phe Ser Glu Asn Ser His Asn Ile Tyr Asn Ala Val His Ala Ile Ala His Ala Leu His Glu Met Asn Leu Gln Gln Ala Asp Asn Gln Ala Ile Asp Asn Gly Lys Gly Ala Ser Ser His Cys Leu Lys Val Asn Ser Phe Leu Arg Arg Thr Tyr Phe Thr Asn Pro Leu Gly Asp Lys Val Phe Met Lys Gln Arg Val Ile Met Gln Asp Glu Tyr.

455 Asp Ile Val His Phe Ala Asn Leu Ser Gln His Leu Gly Ile Lys Met 470 475 Lys Leu Gly Lys Phe Ser Pro Tyr Leu Pro His Gly Arg His Ser His 485 490 Leu Tyr Val Asp Met Ile Glu Leu Ala Thr Gly Arg Arg Lys Met Pro 500 510 505 Ser Ser Val Cys Ser Ala Asp Cys Ser Pro Gly Phe Arg Arg Leu Trp 515 520 Lys Glu Gly Met Ala Ala Cys Cys Phe Val Cys Ser Pro Cys Pro Glu 530 535 540 Asn Glu Ile Ser Asn Glu Thr Asn Met Asp Gln Cys Val Asn Cys Pro 550 555 Glu Tyr Gln Tyr Ala Asn Thr Glu Gln Asn Lys Cys Ile Gln Lys Gly 565 570 Val Thr Phe Leu Ser Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Leu 585 590 Met Ala Phe Cys Phe Ser Ala Phe Thr Ala Val Leu Cys Val Phe 600 605 Val Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ser Leu 615 . 620 Ser Tyr Leu Leu Met Ser Leu Met Phe Cys Phe Leu Cys Ser Phe 630 635 Phe Phe Ile Gly Leu Pro Asn Lys Val Ile Cys Val Leu Gln Gln Ile 645 650 Thr Phe Gly Ile Val Phe Thr Val Ala Val Ser Thr Val Leu Ala Lys 660 665 670 Thr Val Thr Val Val Leu Ala Phe Lys Val Thr Val Pro Gly Arg Arg 675 680 685 Leu Arg Tyr Phe Leu Val Ser Gly Thr Leu Asn Tyr Ile Ile Pro Ile 690 695 700 Cys Ser Leu Leu Gln Cys Val Leu Cys Ala Ile Trp Leu Ala Val Ser 710 715 Pro Pro Phe Val Asp Ile Asp Glu His Ser Gln His Gly His Ile Ile 725 730 Ile Val Cys Asn Lys Gly Ser Val Thr Ala Phe Tyr Cys Val Leu Gly 740 745 Tyr Leu Ala Cys Leu Ala Leu Gly Ser Phe Thr Leu Ala Phe Leu Ala 755 760 Lys Asn Leu Pro Asp Ala Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser 775 Met Leu Val Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr His 790 795 Ser Thr Lys Gly Lys His Met Val Ala Val Glu Ile Phe Ser Ile Leu 805 810 Ala Ser Ser Ala Gly Met Leu Gly Cys Ile Phe Val Pro Lys Ile Tyr 825 830 Ile Ile Leu Met Arg Pro Glu Arg Asn Ser Thr Gln Lys Ile Arg Glu 840 Lys Ser Tyr Phe 850

(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3125 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 1...2169

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(D) OTHER INFORMATION: VR5

(xi) SECUENCE DESCRIPTION: SEC ID N	M7.0.	

	()	(1)	SEQUI	ENCE	DESC	CRIP.	LION	SEÇ	מד נ	NO:	9 :					
			GAA Glu													48
			TCT Ser 20													96
			CTT Leu													144
			CAA Gln													192
			TTG Leu													240
TGG Trp	ATT Ile	GGC Gly	CTT Leu	GTC Val 85	ATC Ile	CCA Pro	GAT Asp	GAC Asp	GAT Asp 90	CAA Gln	GGA Gly	AAC Asn	CAA Gln	TTT Phe 95	CTT Leu	288
			AAG Lys 100													336
			ATA Ile													384
			AAA Lys													432
			ACA Thr													480
			TTA Leu													528
		Ser	AAG Lys 180	Thr	Asp	Ile	Ser	His	Asp	Thr	Phe	Tyr	Gly	Ser		576
ACT Thr	TTT Phe	CTA Leu 195	CCC Pro	CAC His	CAT His	GGT Gly	GAG Glu 200	ATT Ile	TCT Ser	GGC Gly	TTT Phe	AAA Lys 205	AAT Asn	TTT Phe	GTA Val	624
CAG Gln	ACA Thr 210	TGG Trp	TTC Phe	CAT His	CTC Leu	AGA Arg 215	AAC Asn	ACA Thr	GAT Asp	TTA Leu	TAT Tyr 220	CTA Leu	GTA Val	ATG Met	CCA Pro	672
GAG Glu 225	TGG Trp	AAA Lys	TAT	ATT Ile	AAC Asn 230	TCT Ser	GAA Glu	GAC Asp	TCA Ser	GCA Ala 235	TCT Ser	AAT Asn	TGT Cys	AAA Lys	ATA Ile 240	720

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			AGT Ser													768
			ATG Met 260													816
			ATA Ile													864
			GCA Ala													912
			TCC Ser													960
			TTT Phe													1008
			TTT Phe 340													1056
			TTC Phe													1104
			ATG Met													1152
			AGT Ser													1200
			GCA Ala													1248
		Ser	AAT Asn 420	Glu	Thr	Asn	Met	Asp	Gln	Сув	Val	Asn		Pro		1296
Tyr	Gln	Tyr 435	Ala	Asn	Thr	Glu	Gln 440	Asn	Lys	Сув	Ile	Gln 445	Lys	Gly		1344
			AGC Ser												ATG Met	1392
			TTC Phe													1440
			GAC Asp													1488
TAT	CTA	TTA	CTC	ATG	TCA	CTC	ATG	TTC	TGT	TTT	CTG	TGC	TCC	TTT	TTC .	1536

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Tyr	Leu	Leu	Leu 500	Met	Ser	Leu	Met	Phe 505	Сув	Phe	Leu	Cys	Ser 510	Phe	Phe	
TTC Phe	ATT Ile	GGC Gly 515	CTT Leu	CCA Pro	AAC Asn	AAA Lys	GTC Val 520	ATC Ile	TGT Cys	GTC Val	TTA Leu	CAG Gln 525	CAG Gln	ATC Ile	ACA Thr	1584
	GGA Gly 530															1632
GTC Val 545	ACT Thr	GTG Val	GTT Val	CTA Leu	GCT Ala 550	TTC Phe	AAA Lys	GTC Val	ACA Thr	GAC Asp 555	CCA Pro	GGA Gly	AGA Arg	AGA Arg	TTG Leu 560	1680
AGA Arg	TAC Tyr	TTC Phe	CTT Leu	GTA Val 565	TCA Ser	GGG Gly	ACA Thr	CTA Leu	AAC Asn 570	TAC Tyr	ATT Ile	ATT Ile	CCT Pro	ATA Ile 575	TGT Cys	1728
	CTA Leu															1776
CCC Pro	TTT Phe	GTT Val 595	GAT Asp	ATT Ile	GAT Asp	GAA Glu	CAC His 600	TCT Ser	CAG Gln	CAT His	GGC Gly	CAC His 605	ATC Ile	ATC Ile	ATT Ile	1824
GTG Val	TGC Cys 610	AAC Asn	AAG Lys	GGC Gly	TCA Ser	GTT Val 615	ACT Thr	GCA Ala	TTC Phe	TAC Tyr	TGT Cys 620	GTC Val	CTT Leu	GGA Gly	TAC Tyr	1872
TTG Leu 625	GCC Ala	TGC Cys	CTG Leu	GCA Ala	CTG Leu 630	GGA Gly	AGC Ser	TTC Phe	ACT Thr	TTG Leu 635	GCT Ala	TTC Phe	TTG Leu	GCC Ala	AAG Lys 640	1920
	CTG Leu															1968
	GTG Val															2016
ACA Thr	AAG Lys	GGC Gly 675	TÀ2 TY2	CAC His	ATG Met	GTT Val	GCT Ala 680	GTG Val	GAG Glu	ATC Ile	TTC Phe	TCC Ser 685	ATC Ile	TTG Leu	GCA Ala	2064
TCC Ser	AGT Ser 690	GCA Ala	GGG Gly	ATG Met	CTT Leu	GAA Glu 695	Cya	ATT Ile	TTT Phe	GTA Val	CCC Pro 700	AAG Lys	ATT Ile	TAT Tyr	ATC Ile	2112
ATT Ile 705	TTA Leu	ATG Met	AGA Arg	CCA Pro	GAG Glu 710	AGA Arg	AAT Asn	TCT Ser	ACC Thr	CAA Gln 715	AAG Lys	ATC Ile	AGG Arg	GAA Glu	AAA Lys 720	2160
	TAT Tyr		TGA	CAA	ATA 1	TTAC	GAAT	rr cr	GTC	TAAL	TA	\agti	rggt	ACA!	TAACCA	2218
GTGI TCAT CTTC GTTT	ATAAI PTCAC PGTT1 PAATC	AAG (CTT 1 CTG 1 CCA (SAAGT CTTC ATTTC CCACT	PATCA CATT CATGO PTTGO	AT AT TT CT SA GA TG TA	CTAC CTCA CTTGC CAADA	TGAI AGAGI CCT(AAAA	A CTTA A ACT C TGC	TAAAC TAAAC STAAC SATCT	TACA TTCT TTC TAGG	GTGT CTAI CAAI ACAG	CCAT ATTAT AAAC AAAC	TAA 1 TTA (CGT (EGG (AATCT CAATT FGATI FTACI	SCTCTA TTGCAC TTTATT AAGGCA ACATAG AGCAAA	2278 2338 2398 2458 2518 2578

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GTTGAAATCA	GAATTATTTT	CTGATTTCCA	GTAAGAGCAC	ACACAGAAGA	AAATACTGAC	2638
TTTTTTTTTC	TTCTGTTCTT	CAAGCTACTG	GCCAATAATC	TAAGGAGGAA	ATGTTCCTTT	2698
TCTGCTGTCA	AATACAAATA	TATTATATCC	AACAATGATC	AGAAGCCCAG	GGATTCTGTG	2758
GCTGAATTGG	GAATATTTGG	AAGAAGCTGA	GGAGGAGGGT	GACCAGCATT	CTCAACAAAC	2818
CTGGACAAGC	AAGATCTCTC	AGACACTGAG	CCTCTAACCA	GAGATCATAC	ACAAGCTGAT	2878
GTGAAGCCCC	CAACAAATAT	GCACCATAAG	ACTGCCTGGT	CTAGCATCAG	TGGGAGACAC	2938
ACCTAACCCC	AGAGAGACTT	AAGTCCCCAG	GGATTGGGAA	GTGCTGGGCA	TTGAGGATGT	2998
AGGGATATCA	TCTTTGAGAT	GGCAGAGGAG	TTGTTAGATG	AGGAAGAGTC	AGGGGGGCAA	3058
ACCAGGAAGG	GGATAACTAC	TAGATTGTAA	CAAAAATATT	GAGTAATAAT	AAATTAAAA	3118
ATGAAAT						3125

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 723 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Ile Cys Asn Glu Glu Ser Met Cys Ser Phe Leu Leu Ser Gly Pro Asn 10 Trp Asp Glu Ser Leu Ser Phe Trp Lys Tyr Leu Asp Ser Phe Leu Ser . 20 Pro His Ile Leu Gln Leu Ser Tyr Gly Ser Phe Ser Ser Ile Phe Ser 40 45 Asp Asp Glu Gln Tyr Pro Tyr Leu Tyr Gln Met Ala Pro Lys Asp Thr 55 Ser Leu Ala Leu Ala Met Val Ser Phe Ile Leu Tyr Leu Lys Trp Asn 70 75 Trp Ile Gly Leu Val Ile Pro Asp Asp Asp Gln Gly Asn Gln Phe Leu 85 90 Leu Glu Leu Lys Lys Gln Ser Glu Asn Lys Glu Ile Cys Phe Ala Phe 100 105 110 Val Lys Met Ile Ser Val Asp Glu Val Ser Phe Pro Gln Lys Thr Glu 115 120 125 Ile Tyr Tyr Lys Gln Ile Val Lys Ser Leu Thr Asn Val Ile Ile Ile 130 135 140 Tyr Gly Glu Thr Tyr Asn Phe Ile Asp Leu Ile Phe Arg Met Trp Glu 150 155 Pro Pro Ile Leu Gln Arg Ile Trp Ile Thr Thr Lys Gln Leu Asn Phe 165 170 Pro Thr Ser Lys Thr Asp Ile Ser His Asp Thr Phe Tyr Gly Ser Leu 180 185 190 Thr Phe Leu Pro His His Gly Glu Ile Ser Gly Phe Lys Asn Phe Val 200 205 Gln Thr Trp Phe His Leu Arg Asn Thr Asp Leu Tyr Leu Val Met Pro 215 220 Glu Trp Lys Tyr Ile Asn Ser Glu Asp Ser Ala Ser Asn Cys Lys Ile 230 235 Leu Lys Asn Ser Ser Ser Asp Ala Ser Phe Asp Trp Leu Met Glu Gln 245 250 255 Lys Leu Asp Met Ala Phe Ser Asp Asn Ser His Asn Ile Tyr Asn Val 260 265 270 Val His Ala Ile Ala His Ala Leu His Glu Met Asn Leu Gln Gln Ala 275 280 285 Asp Asn Gln Ala Ile Asp Asn Gly Lys Gly Ala Ser Ser His Cys Leu 290 295 300 Lys Val Asn Ser Phe Leu Arg Arg Thr Tyr Phe Thr Asn Pro Leu Gly 310 315 Asp Lys Val Phe Met Lys Gln Arg Val Ile Met Gln Asp Glu Tyr Asp.

330 325 Ile Val His Phe Ala Asn Leu Ser Gln His Leu Gly Ile Lys Met Lys 340 345 350 Leu Gly Lys Phe Ser Pro Tyr Leu Pro His Gly Arg His Ser His Leu 355 360 365 Tyr Val Asp Met Ile Glu Leu Ala Thr Gly Arg Arg Lys Met Pro Ser 375 370 380 Ser Val Cys Ser Ala Asp Cys Ser Pro Gly Phe Arg Arg Leu Trp Lys 390 395 Glu Gly Met Ala Ala Cys Cys Phe Val Cys Ser Pro Cys Pro Glu Asn 405 410 Glu Ile Ser Asn Glu Thr Asn Met Asp Gln Cys Val Asn Cys Pro Glu 425 420 Tyr Gln Tyr Ala Asn Thr Glu Gln Asn Lys Cys Ile Gln Lys Gly Val 440 Thr Phe Leu Ser Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Leu Met 455 460 Ala Phe Cys Phe Ser Ala Phe Thr Ala Val Val Leu Cys Val Phe Val 470 475 Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ser Leu Ser 485 490 Tyr Leu Leu Met Ser Leu Met Phe Cys Phe Leu Cys Ser Phe Phe 505 Phe Ile Gly Leu Pro Asn Lys Val Ile Cys Val Leu Gln Gln Ile Thr 515 520 525 Phe Gly Ile Val Phe Thr Val Ala Val Ser Thr Val Leu Ala Lys Thr 540 530 535 Val Thr Val Val Leu Ala Phe Lys Val Thr Asp Pro Gly Arg Arg Leu 550 555 Arg Tyr Phe Leu Val Ser Gly Thr Leu Asn Tyr Ile Ile Pro Ile Cys 570 565 Ser Leu Leu Gln Cys Val Leu Cys Ala Ile Trp Leu Ala Val Ser Pro 580 585 590 Pro Phe Val Asp Ile Asp Glu His Ser Gln His Gly His Ile Ile Ile 595 600 605 Val Cys Asn Lys Gly Ser Val Thr Ala Phe Tyr Cys Val Leu Gly Tyr 610 620 Leu Ala Cys Leu Ala Leu Gly Ser Phe Thr Leu Ala Phe Leu Ala Lys 630 635 Asn Leu Pro Asp Ala Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met 645 650 Leu Val Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr His Ser 660 665 670 Thr Lys Gly Lys His Met Val Ala Val Glu Ile Phe Ser Ile Leu Ala 675 680 685 Ser Ser Ala Gly Met Leu Glu Cys Ile Phe Val Pro Lys Ile Tyr Ile 695 700 Ile Leu Met Arg Pro Glu Arg Asn Ser Thr Gln Lys Ile Arg Glu Lys 710 Ser Tyr Phe

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1889 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAATTCGGCT TCTGCACCAA ATGGCGACGA AAGACACATC TCTTTCACTT GCCATTGTTT 60 CTTTGATGGT TCATTTTAGG TGGTCTTGGG TTGGTCTAAT TCTCCCAGAT GACCACAAAG 120 GAAATAAAAT ACTATCAGAT TTTAGAAAGG AGATGGAAAG AAAAAGAATC TGTACGGCTT TTGTAAAAAT GATTCCTGCC ACATGGACTT CATCTTTTGT CAAATTCTGG GAAAATATGG 240 ATGACACCAA CATAATAATT ATTTATGGTG ACATTGATTC TCTAGAAGGT CTAATGCGAA 300 ATATTGGGCA AAGGTTATTG ACATGGCATG TCTGGGTCAT GAACATTGAA CCCCATATTA TTGAATATGA TAATTATTTC ATGTTAGATT CATTCCATGG AAGTTTAATT TTTAAGCACA 420 ATTATAGAGA GAATTTTGAG TTTACCAAAT TTATTCGAAC AGTTAATCCT AAAAAATACC CAGAAGACAT TTATCTCCCT AAGATGTGGT ATTTGTTCTT CATGTGCTCA TTTTCTGATA 540 TTAATTGTCA AGTTTTGGAC AGCTGTCAAA CAAATGCTTC TTTGGATATG TTACCTAGTC AGATATTTGA TGTGGTCATG AGTGAAGAGA GCACAAGTAT TTACAATGCT GTGTACGCTG 660 TGGCTCACAG CCTCCATGAG ATGAGACTTC AGCAACTTCA AACACAACCG TGTGAAAATG AAGAAGGGAT GGAGTTCTTT CCATGGCAGC TTAATACTTT CCTGAAGGAT ATTGAGGTGA 780 GAGTCAACAG TTTAGACTGG AGACAGAGAA TAGATGCTGA ATATGACATT CTTAACCTCT GGAATTTACC AAAGGGTCTT GGACTAAAAG TGAAAATAGG AAACTTTTAT GCAAATGCTC 900 CCCAGGGTCA ACAATTGTCT TTATCTGAAC AGATGATTCA ATGGCCAGAA ATATTTTCAG AGATCCCTCA GTCGGTGTGC AGTGAGAGTT GTGGGCCTGG ATTCAGGAAA GTAACCCTGG 1020 AGAATAAGGC TATCTGCTGC TACAATTGTA CTCCCTGTGC AGACAATGAG ATTTCTAATG AGACAGATGT AGACCAGTGT GTGAAGTGTC CAGAGAGTCA TTATGCAAAT ACAGAGAAGA GCAACTGCTA TCAAAAGTCT GTGAGCTTTC TGGGCTATGA AGACCCTTTG GGGATGGCTC TAGCCAGCAT AGCTTTGTGC TTGTCTGCAC TAACTGCCTT TGTTATTGGC ATATTTGTGA AACACAAAGA CACTCCTATT GTTAAGGCCA ATAATCAAGC TCTGAGTTAC ACTTTGCTCA 1320 TCACACTCAA ATTCTGTTTC CTATGTTCTT TGAACTTCAT TGGTCAGCCC AACACAGTTG CCTGCATCCT TCAGCAGACC ACCTTTGCAG TTGCTTTCAC TATGGCTCTT GCCACTGTGT TGGCCAAAGC TATCACTGTG GTTCTTGCCT TTAAGGTCAG TTTTCCAGGG AGAATGGTAA GATGGCTAAT GATATCAAGG GGTCCAAACT ATATCATTCC TATCTGCACC CTGATCCAAC 1560 TTCTTCTTTG TGGAATATGG ATGGCAATAT CTCCACCATA CATTGACCAA GATGCTCATA TTGAACATGG TCACATCATC ATTTTGTGCA ACAAGGGCTC AGCTGTTGCC TTCCACTCTG 1680 TCCTGGGATA CCTCTGCTTC TTGGCCCTTG GGAGTTATAC CATGGCCTTC TTGTCAAGAA ATTTGCCTGA TACATTCAAC GAATCCAAAT TTATCTCACT AAGTATGCTG GTATTCTTCT 1800 GTGTCTGGAT CACCTTTCTT CCTGTCTACC ACAGCACTAA AGGGAAGGTC ATGGTCGCCG 1860 TCGAGGTCTT TTGCATCCAA GCCGAATTC 1889

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 604 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Ser Leu Ser Leu Ala Ile Val Ser Leu Met Val His Phe Arg Trp Ser 10 Trp Val Gly Leu Ile Leu Pro Asp Asp His Lys Gly Asn Lys Ile Leu 20 25 Ser Asp Phe Arg Lys Glu Met Glu Arg Lys Arg Ile Cys Thr Ala Phe 40 Val Lys Met Ile Pro Ala Thr Trp Thr Ser Ser Phe Val Lys Phe Trp 55 60 Glu Asn Met Asp Asp Thr Asn Ile Ile Ile Ile Tyr Gly Asp Ile Asp Ser Leu Glu Gly Leu Met Arg Asn Ile Gly Gln Arg Leu Leu Thr Trp 85 90 His Val Trp Val Met Asn Ile Glu Pro His Ile Ile Glu Tyr Asp Asn 105 100 Tyr Phe Met Leu Asp Ser Phe His Gly Ser Leu Ile Phe Lys His Asn 120 Tyr Arg Glu Asn Phe Glu Phe Thr Lys Phe Ile Arg Thr Val Asn Pro 130 135 140 Lys Lys Tyr Pro Glu Asp Ile Tyr Leu Pro Lys Met Trp Tyr Leu Phe 150 155

Phe Met Cys Ser Phe Ser Asp Ile Asn Cys Gln Val Leu Asp Ser Cys Gln Thr Asn Ala Ser Leu Asp Met Leu Pro Ser Gln Ile Phe Asp Val Val Met Ser Glu Glu Ser Thr Ser Ile Tyr Asn Ala Val Tyr Ala Val Ala His Ser Leu His Glu Met Arg Leu Gln Gln Leu Gln Thr Gln Pro Cys Glu Asn Glu Glu Gly Met Glu Phe Phe Pro Trp Gln Leu Asn Thr Phe Leu Lys Asp Ile Glu Val Arg Val Asn Ser Leu Asp Trp Arg Gln Arg Ile Asp Ala Glu Tyr Asp Ile Leu Asn Leu Trp Asn Leu Pro Lys Gly Leu Gly Leu Lys Val Lys Ile Gly Asn Phe Tyr Ala Asn Ala Pro Gln Gly Gln Gln Leu Ser Leu Ser Glu Gln Met Ile Gln Trp Pro Glu Ile Phe Ser Glu Ile Pro Gln Ser Val Cys Ser Glu Ser Cys Gly Pro Gly Phe Arg Lys Val Thr Leu Glu Asn Lys Ala Ile Cys Cys Tyr Asn Cys Thr Pro Cys Ala Asp Asn Glu Ile Ser Asn Glu Thr Asp Val Asp Gln Cys Val Lys Cys Pro Glu Ser His Tyr Ala Asn Thr Glu Lys Ser Asn Cys Tyr Gln Lys Ser Val Ser Phe Leu Gly Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Ser Ile Ala Leu Cys Leu Ser Ala Leu Thr Ala Phe Val Ile Gly Ile Phe Val Lys His Lys Asp Thr Pro Ile Val Lys Ala Asn Asn Gln Ala Leu Ser Tyr Thr Leu Leu Ile Thr Leu Lys Phe Cys Phe Leu Cys Ser Leu Asn Phe Ile Gly Gln Pro Asn Thr Val Ala Cys Ile Leu Gln Gln Thr Thr Phe Ala Val Ala Phe Thr Met Ala Leu Ala Thr Val Leu Ala Lys Ala Ile Thr Val Val Leu Ala Phe Lys Val Ser Phe Pro Gly Arg Met Val Arg Trp Leu Met Ile Ser Arg Gly Pro Asn Tyr Ile Ile Pro Ile Cys Thr Leu Ile Gln Leu Leu Cys Gly Ile Trp Met Ala Ile Ser Pro Pro Tyr Ile Asp Gln Asp Ala His Ile Glu His Gly His Ile Ile Ile Leu Cys Asn Lys Gly Ser Ala Val Ala Phe His Ser Val Leu Gly Tyr Leu Cys Phe Leu Ala Leu Gly Ser Tyr Thr Met Ala Phe Leu Ser Arg Asn Leu Pro Asp Thr Phe Asn Glu Ser Lys Phe Ile Sér Leu Ser Met Leu Val Phe Phe Cys Val Trp Ile Thr Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys Val

(2) INFORMATION FOR SEQ ID NO:13:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1889 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

GAATTCGGCT	TCTGCATCAA	ATGGCGACGA	AGGACACATC	TCTTTCACTT	GCCATTGTTT	60
CTTTGATGGT	TCATTTTAGG	TGGTCTTGGG	TTGGTCTAAT	TCTCCCAGAT	GACCACAAAG	120
GAAATAAAAT	ACTATCAGAT	TTTAGAAAGG	AGATGGAGAG	AAAAAGAATC	TGTACGGCTT	180
TTGTAAAAAT	GATTCCTGCC	ACATGGACTT	CATCTTTTGT	CAAATTCTGG	GAAAATATGG	240
ATGACACCAA	CATAATAATT	ATTTATGGTG	ACATTGATTC	TCTAGAAGGT	CCAATGCGAA	300
ATATTGGGCA	AAGGTTATTG	ACATGGCATG	TCTGGGTCAT	GAACATTGAA	CCCCATATTA	360
TTGAATATGA	TAATTATTTC	ATGTTAGATT	CATTCCATGG	AAGTTTAATT	TTTAAGCACA	420
ATTATAGAGA	GAATTTTGAG	TTTACCAAAT	TTATTCGAAC	AGTTAATCCT	AAAAAATACC	480
CAGAAGACAT	TTATCTCCCT	AAGATGTGGT	ATTTGTTCTT	CATGTGCTCA	TTTTCTGATA	540
TTAATTGTCA	AGTTTTGGAC	AGCTGTCAAA	CAAATGCTTC	TTTGGATATG	TTACCTAGTC	600
AGATATTTGA	TGTGGTCATG	AGTGAAGAGA	GCACAAGTAT	TTACAATGCT	GTGTACGCTG	660
TGGCTCACAG	CCTCCATGAG	ATGAGACTTC	AGCAACTTCA	AACACAACCG	TGTGAAAATG	720
AAGAAGGGAT	GGAGTTCTTT	CCATGGCAGC	TTAATACTTT	CCTGAAGGAT	ATTGAGGTGA	780
GAGTCAACAG	TTTGGACTGG	AGACAGAGAA	TAGATGCTGA	ATATGACATT	CTTAACCTCT	840
GGAATTTACC	AAAGGGTCTT	GGACTAAAAG	TGAAAATAGG	AAACTTTTAT	GCAAATGCTC	900
CCCAGGGTCA	ACAATTGTCT	TTATCTGAAC	AGATGATTCA	ATGGCCAGAA	ATATTTTCAG	960
AAGTCCCTCA	GTCTGTGTGC	AGTGAGAGTT	GTAGGCCTGG	ATTCAGGAAA	GTATCCCTGG	1020
ATGATAAGGC	CATCTGCTGC	TACAAGTGCA	CTCCTTGTGC	CGACAATGAG	ATATCTAATG	1080
AGACAGATGT	AGACCAGTGT	GTGAAGTGTC	CAGAGAGTCA	TTATGCAAAT	ACAGAGAAGA	1140
GCAACTGCTT	CCCAAAATCT	GTGAGCTTTC	TGGCCTATGA	AGACCCCTTG	GGGATGGCTC	1200
TAGCCAGCAT	AGCTTTGTGC	TTATCTGCAC	TCACTGTCTT	TGTTATTGGC	ATCTTTGTGA	1260
AAAACAGAGA	CACTCCTATT	GTCAAGGCCA	ATAATCGGAC	TCTAAGTTAC	ATTTTGCTCA	1320
TCACACTCAC			TGAACTTCAT	TGGTCAGCCC	AACACAGCTG	1380
CCTGCATCCT	TCAGCAGACC	ACCTTTGCAG	TTGCTTTCAC	TATGGCTCTT	GCCACTGTGT	1440
TGGCCAAAGC	TATTACTGTA		TTAAGATCAG	TTTTCCAGGG	AGAATGTTAA	1500
GGTGGCTAAT	GATATCAAGG	GGTCCAAGAT	ACATCATTCC	TATCTGCACA	CTGATCCAGC	1560
TTCTTCTTTG	TGGAATATGG	ATGGCAACTT	CTCCACCATT	CATTGACCAA	GATGTTAATA	1620
CTGAAGATGG	ATACATCATC	CTTTTGTGCA	ACAAGGGCTC	AGCTGTTGCC	TTCCATTCAG	1680
	CCTCTGTTTC	TTGGCCCTTG	GGAGTTATAC	CATGGCCTTC	TTGTCTAGAA	1740
ATTTGCCTGA		GAATCCAAAT		CAGTATGCTG	GTGTTCTTCT	1800
GTGTCTGGGT	CACCTTTCTT	CCTGTCTACC	ACAGCACTAA	AGGGAAAGTT	ATGGTCGTCG	1860
TCGAAGTCTT	CTGCATCCAA	GCCGAATTC				1889

(2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 604 amino acids
 (B) TYPE: amino acid

 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Ser Leu Ser Leu Ala Ile Val Ser Leu Met Val His Phe Arg Trp Ser 10 15 Trp Val Gly Leu Ile Leu Pro Asp Asp His Lys Gly Asn Lys Ile Leu 20 25 Ser Asp Phe Arg Lys Glu Met Glu Arg Lys Arg Ile Cys Thr Ala Phe 35 40 Val Lys Met Ile Pro Ala Thr Trp Thr Ser Ser Phe Val Lys Phe Trp 55 Glu Asn Met Asp Asp Thr Asn Ile Ile Ile Ile Tyr Gly Asp Ile Asp 70 Ser Leu Glu Gly Pro Met Arg Asn Ile Gly Gln Arg Leu Leu Thr Trp 85 90 His Val Trp Val Met Asn Ile Glu Pro His Ile Ile Glu Tyr Asp Asn 100 105

Tyr Phe Met Leu Asp Ser Phe His Gly Ser Leu Ile Phe Lys His Asn Tyr Arg Glu Asn Phe Glu Phe Thr Lys Phe Ile Arg Thr Val Asn Pro Lys Lys Tyr Pro Glu Asp Ile Tyr Leu Pro Lys Met Trp Tyr Leu Phe Phe Met Cys Ser Phe Ser Asp Ile Asn Cys Gln Val Leu Asp Ser Cys Gln Thr Asn Ala Ser Leu Asp Met Leu Pro Ser Gln Ile Phe Asp Val Val Met Ser Glu Glu Ser Thr Ser Ile Tyr Asn Ala Val Tyr Ala Val Ala His Ser Leu His Glu Met Arg Leu Gln Gln Leu Gln Thr Gln Pro Cys Glu Asn Glu Glu Gly Met Glu Phe Phe Pro Trp Gln Leu Asn Thr Phe Leu Lys Asp Ile Glu Val Arg Val Asn Ser Leu Asp Trp Arg Gln Arg Ile Asp Ala Glu Tyr Asp Ile Leu Asn Leu Trp Asn Leu Pro Lys Gly Leu Gly Leu Lys Val Lys Ile Gly Asn Phe Tyr Ala Asn Ala Pro Gln Gly Gln Gln Leu Ser Leu Ser Glu Gln Met Ile Gln Trp Pro Glu Ile Phe Ser Glu Val Pro Gln Ser Val Cys Ser Glu Ser Cys Arg Pro Gly Phe Arg Lys Val Ser Leu Asp Asp Lys Ala Ile Cys Cys Tyr Lys Cys Thr Pro Cys Ala Asp Asn Glu Ile Ser Asn Glu Thr Asp Val Asp Gln Cys Val Lys Cys Pro Glu Ser His Tyr Ala Asn Thr Glu Lys Ser Asn Cys Phe Pro Lys Ser Val Ser Phe Leu Ala Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Ser Ile Ala Leu Cys Leu Ser Ala Leu Thr Val Phe Val Ile Gly Ile Phe Val Lys Asn Arg Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Thr Leu Ser Tyr Ile Leu Leu Ile Thr Leu Thr Phe Cys Phe Leu Cys Ser Leu Asn Phe Ile Gly Gln Pro Asn Thr Ala Ala Cys Ile Leu Gln Gln Thr Thr Phe Ala Val Ala Phe Thr Met Ala Leu Ala Thr Val Leu Ala Lys Ala Ile Thr Val Val Leu Ala Phe Lys Ile Ser Phe Pro Gly Arg Met Leu Arg Trp Leu Met Ile Ser Arg Gly Pro Arg Tyr Ile Ile Pro Ile Cys Thr Leu Ile Gln Leu Leu Cys Gly Ile Trp Met Ala Thr Ser Pro Pro Phe Ile Asp Gln Asp Val Asn Thr Glu Asp Gly Tyr Ile Ile Leu Leu Cys Asn Lys Gly Ser Ala Val Ala Phe His Ser Val Leu Gly Tyr Leu Cys Phe Leu Ala Leu Gly Ser Tyr Thr Met Ala Phe Leu Ser Arg Asn Leu Pro Asp Thr Phe Asn Glu Ser Lys Phe Leu Ser Phe Ser Met Leu Val Phe Phe Cys Val Trp Val Thr Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys Val

(2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 2561 base pairs (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA
 (ix) FEATURE: (A) NAME/KEY: Coding Sequence (B) LOCATION: 80...349 (D) OTHER INFORMATION: VR8
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ATAGGTGCAA CTGTGTGTGT GATGTTTTC TACATCAGAA ACGGATTTCA CAACAGCTCC ATCTTAGATC CTAGCAGAC ATG AAG AAG CTC TGT GCT TTC ACG ATT TCA TTG Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Leu 1 5 10	60 112
TTG TTT CTG AAG TTT TCT CTC ATC TTG TGC TGT TGG AGT GAA CCA AGT Leu Phe Leu Lys Phe Ser Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser 15 20 25	160
TGC TTT TGG AGG ATA AAG AAT AGT GAT GAT AAT GAC GGA GAT TTG CAA Cys Phe Trp Arg Ile Lys Asn Ser Asp Asp Asn Asp Gly Asp Leu Gln 30 35 40	208
AGG GAA TGT CAT TTT TAC CTT GGG GCA GCT GAT ACA CCA GTT GAA GAT Arg Glu Cys His Phe Tyr Leu Gly Ala Ala Asp Thr Pro Val Glu Asp 45 50 55	256
AAT TTT TAT AGT TCA CTT TTA AAA TTT AGG TTT TCT TTG GAC CAT TTA Asn Phe Tyr Ser Ser Leu Leu Lys Phe Arg Phe Ser Leu Asp His Leu 60 70 75	304
ATC CTA ACC TAC GCG ACC ATG ACC GGC TGC CCC ATG TCC ATC AGG TAGCC Ile Leu Thr Tyr Ala Thr Met Thr Gly Cys Pro Met Ser Ile Arg 80 85 90	354
CCCAAGGACA CACATTTGTC CCATGGCATG GTCTCCTTGA TGTTTCACTT TAGATGGACT	414
TGGATAGGAA TGGTCATCTC AGATGATGAC CAGGGTATTC AGTTTCTCTC AGATTTAAGA	474
GAAGAAAGCC AAAGGCATGG GATCTGTTTA GCTTTTGTTA ATATGATCCC AGAAAACATG	534
CAGATATACA TGACAAGGGC TACAATATAT GATCAACAAA TTATGACATC TTCAGCAAAG	594
GTTGTTATCA TTTATGGTGA AATGAACTCT ACTCTAGAAG TAAGCTTTAG AAGATGGGAA	654
GAGTTAGGTG CTCGGAGAAT CTGGATCACA ACCTCACAAT GGGATGTCAT CACAAATAAA	714
ARAGACTTCA CCCTTAATCT CTTCCATGGG ACTATCACTT TTGCACACCA CAGAGTTGAG	774
ATTCCTAAAT TAAATAAATT CATGCAAACA ATGAACACTG CCAAATACCC AGTAGATATT	834
TCTCATACTA TATTGGAGTG GAATTATTTT AATTGTTCAA TATCTAAGAA CAGCATTAGA	894
ATGCATCATA TTACATTCAA CAACACCTTG GAATGGACAT CACTGCACAA CTATGATATG	954
GCGATGAGTG ATGAAGGTTA CAGTTTATAT AATGCTGTTT ATGCTGTGGC CCACACCTAC	1014
CATGAATACA TTTTTCAACA AGTAGAGTCT CAGAAAAAGG CAAAACCCAA AAGATATTTC	1074
ACTGCTTGTC AGCAGCCTCA GGTTCCCTCC TCCGTGTGTA GTGTGGCATG TACTGCTGGA TTCAGGAAAA TTTATCAAAA AGAAACAGCA GACTGCTGCT TTGATTGTGT TCAGTGCCCA	1134 1194
GAAAATGAGA TTTCCAACGA AACAGATATG GAACAGTGTG TGAGGTGTCC AGATGATAAG	1254
TATGCCAACA TAGAGCAAAC CCACTGCCTC TCAAGAGCTG TATCATTTCT GGCTTATGAA	1314
GATCCATTGG GGATGGCTCT AGGCTGCATG GCACTGTCCT TCTCGGCCAT CACAATTCTA	1374
GTCCTCGTCA CATTTGTGAA ACACAACGAT ACTCCCATTG TGAAGGCCAA TAACCGCATT	1434
CTCAGCTACA TCCTGCTCAT CTCTCTCGTC TTCTGCTTTC TCTGCTCCCT GCTCTTCATT	1494
GGACCTCCCG ACCAGGTCAC CTGCATCTTG CAGCAGACCA CATTTGGAGT ATTTTTCACT	1554
GTGTCTGTTT CTACAGTGTT GGCCAAAACA ATAACTGTGG TCATGGCTTT CAAGCTCACT	1614
ACTCCAGGAA GAAGGATGAG AGGGATGATG ATGACAGGGG CACCTAAGTT GGTCATTCCC	1674
ATTTGTACCC TGATCCAACT TGTTCTCTGT GGAATCTGGT TGGTCACATC TCCTCCCTTT	1734
ATTGACAGAG ATATACAATC TGAGCATGGG AAGATTGTCA TTCTTTGCAA TAAAGGCTCA	1794

GTCATTGCCT	TCCACGTCGT	CCTGGGATAC	TTGGGCTCCT	TGGCTCTGGG	GAGCTTCACT	1854
TTGGCTTTCT	TGGCTAGGAA	CCTTCCTGAC	ACATTCAATG	AAGCCAAGTT	CCTAACTTTC	1914
AGCATGCTGG	TGTTCTGCAG	TGTCTGGATC	ACCTTCCTCC	CTGTCTACCA	CAGCACCAGG	1974
GGGAGGGTCA	TGGTGGTTGT	GGAGGTTTTC	TCCATCTTGG	CTTCTAGTGC	AGGGTTGCTA	2034
ATGTGTATCT	TTGTCCCAAA	GTGTTATGTT	ATTTTAATTA	GACCAGATTC	AAATATTATA	2094
AAGAAACATA	AAGGTAAAGT	GCTTAATTGA	AACTTTCATG	GTATGAAAAT	GTTAGATGAT	2154
ATTCAACTTA	TCTTATTCTT	CATCTTAATA	AAAGCAGTAC	TTCATCATAT	AAAAAATAAA	2214
GTAATATACA	GATTTATACT	TACAAACTGG	ACAGCAAACA	TGAATATGTT	GAGAACTGGG	2274
ATTCTCAATT	GAGGAATGGC	TACCAACATT	TTGATCTGTG	GTTTTGTGTT	TAAGCCATGC	2334
ACTTAATTAA	TGATTAACAT	GAGGTTACCC	TACTGTCTGT	GAACAGCGCC	ACCTCTAGGC	2394
ATGCTGTCCT	TGAGTTATAA	GAAAGGGTAC	TGCATACACA	ATGGACATGA	AGCCAGTAAT	2454
CAACATTATT	CCACTTGCTT	TCATGGAGTT	CTTACTTCCA	AGTTCATGCC	TTGACTTTAT	2514
TCAATGTTCT	ATGACAAAGG	TAGATAAATA	AATAAACACT	TTTCCTC		2561

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 90 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Leu Leu Phe Leu Lys Phe 10 Ser Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser Cys Phe Trp Arg Ile . 30 25 20 Lys Asn Ser Asp Asp Asn Asp Gly Asp Leu Gln Arg Glu Cys His Phe 40 45 35 Tyr Leu Gly Ala Ala Asp Thr Pro Val Glu Asp Asn Phe Tyr Ser Ser 55 Leu Leu Lys Phe Arg Phe Ser Leu Asp His Leu Ile Leu Thr Tyr Ala 70 Thr Met Thr Gly Cys Pro Met Ser Ile Arg 85

(2) INFORMATION FOR SEQ ID NO:17:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2734 base pairs
 - (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 80...1387
 - (D) OTHER INFORMATION: VR9
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ATAGGTGCAA CTGTGTGTGT GATGTTTTTC TACATCAGAA ACGGATTTCA CAACAGCTCC

ATCTTAGATC CTAGCAGAC ATG AAG AAG CTC TGT GCT TTC ACG ATT TCA TTG

Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Leu

1 5 10

TTG TTT CTG AAG TTT TCT CTC ATC TTG TGC TGT TGG AGT GAA CCA AGT
Leu Phe Leu Lys Phe Ser Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser.

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	15	•			20			25				
									TTG Leu		2	808
									GAA Glu		2	256
									GAA Glu		3	304
 							 -		AGG Arg 90		3	352
				Thr					GGT Gly		4	100
									CAA Gln		4	148
									GAT Asp		4	196
									AAA Lys		5	544
									AAT Asn 170		5	592
									GCC Ala		(640
									CAC His		•	688
									GGT Gly		•	736
									ATC Ile		,	784
									ATG Met 250		1	832
									AAG Lys			880
					Ser			Ser		AGA Arg		928

															TCA Ser		976
•															TTC Phe		1024
	GGG Gly	ACT Thr	ATC Ile	ACT Thr	TTT Phe 320	GCA Ala	CAC His	CAC His	AGA Arg	GTT Val 325	GAG Glu	ATT Ile	CCT Pro	AAA Lys	TTA Leu 330	AAT Asn	1072
															ATT Ile		1120
															AAG Lys		1168
															TGG Trp		1216
															AGT Ser		1264
															ATT Ile 410		1312
															TTC Phe		1360
				CAG Gln						TGAC	GTG	rcc 1	\GAT(LATAE	AG T	ATGCCA	1414
	רמים	ראמאמ	מסב	ארכנ	ים כידר	בר כי	וריייים	אמאנ	ב כידו	ייי מייני	ידיידיעי	The Cartie	عريرسوم	ייי מיי	בא א כי	ATCCAT	1474
																CCTCG	1534
																CAGCT	1594
	ACAT	CCTC	GCT (CATC	CTC	rc G	CTT	TGC	TT	CTCTC	CTC	CCTC	CTC	TTC A	ATTGO	BACCTC	1654
																CTCTG	1714
																CTCCAG	1774
																TTGTA	1834
	CCCI	GAT(יייי גייי	CA	ACTLIA CALIA	iTTC?	יים איני איני איני	oTGG!	ATC	r GG?	TIGGT	CAC	ATCI	CCTC	CC 1	rara?	TGACA CATTG	1894
	CCLL	CCAC	CGT (CGTC	これらにい	ידי בני	AGANA AGANA	ませばしし 3WT T.C	י בכיי דכז	ביי זיכן	י די זיפי	CAA	S D CICLO	ייירט ז דיריי	T CNG.	rCATTG rGGCTT	1954 2014
	TCT	rGGC	rag (BAAC	TTC	T G	ACAC	ATTC	ATO	BAAG	CAA	GTT	CTA	ACT T	TCAC	CATGC	2074
																GAGGG	2134
																ATDTD	2194
	TCT	TGT	CCC 1	\AAG1	rgtt <i>i</i>	AT G	TAT:	TTA	A TT	AGAC	AGA	TTC	LAAT	ATT A	ATAA	AGAAAC	2254
	ATA	AGG!	CAA A	AGTG	CTTAL	AT TO	JAAAE	CTTT	ATO	GTA	GAA	AATO	TTAC	SAT (GATA!	TCAAC	2314
	TIM	: CT.T.	י העלט דדי (OT LCA	י מ מייני	LA A.	CANA	AGCA(או ב	TTC/	AUCA	CTT	י מב <i>ו</i> מב מבומב	AAT A	HAAG'	TATAT	2374 2434
	ATTO	AGG	AT (GCT	ACCA	AC A	TTTT	BATC	CTO	GTT1	TCT	GTT	LYDU	CA	rgca:	TAAT	2494
																GCTGT	2554
																ACATT	2614
																CAATGT	2674
	TCT	ATGAC	CAA A	AGGT	AGATA	AA A	CAAA?	DAAAT	C AC	rttc	CTCA	CAA	LAAA	AAA A	LAAAA	AAAAA	2734
					•												2734

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 436 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Leu Leu Phe Leu Lys Phe Ser Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser Cys Phe Trp Arg Ile Lys Asn Ser Asp Asp Asn Asp Gly Asp Leu Gln Arg Glu Cys His Phe Tyr Leu Gly Ala Ala Asp Thr Pro Val Glu Asp Asn Phe Tyr Ser Ser Leu Leu Lys Phe Arg Ile Ala Ala Ser Glu Tyr Glu Phe Leu Leu Val Met Phe Phe Ala Ile Asp Glu Ile Asn Arg Asn Pro Tyr Leu Leu Pro Asn Ile Thr Leu Met Phe Ser Phe Ile Gly Gly Asn Cys Gln Asp Leu Leu Arg Val Met Asp Gln Ala Tyr Thr Gln Ile Asn Gly His Met Asn Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Ala Ile Gly Leu Thr Gly Pro Ser Trp Lys Thr Ser Leu Lys Leu Ala Met His Ser Ser Met Pro Leu Val Phe Phe Gly Pro Phe Asn Pro Asn Leu Arg Asp His Asp Arg Leu Pro His Val His Gln Val Ala Pro Lys Asp Thr His Leu Ser His Gly Met Val Ser Leu Met Phe His Phe Arg Trp Thr Trp Ile Gly Met Val Ile Ser Asp Asp Asp Gln Gly Ile Gln Phe Leu Ser Asp Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr Asp Gln Gln Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly Glu Met Asn Ser Thr Leu Glu Val Ser Phe Arg Arg Trp Glu Glu Leu Gly Ala Arg Arg Ile Trp Ile Thr Thr Ser Gln Trp Asp Val Ile Thr Asn Lys Lys Asp Phe Thr Leu Asn Leu Phe His Gly Thr Ile Thr Phe Ala His His Arg Val Glu Ile Pro Lys Leu Asn Lys Phe Met Gln Thr Met Asn Thr Ala Lys Tyr Pro Val Asp Ile Ser His Thr Ile Leu Glu Trp Asn Tyr Phe Asn Cys Ser Ile Ser Lys Asn Ser Ile Arg Met His His Ile Thr Phe Asn Asn Thr Leu Glu Trp Thr Ser Leu His Asn Tyr Asp Met Ala Met Ser Asp Glu Gly Tyr Ser Leu Tyr Asn Ala Val Tyr Ala Val Ala His Thr Tyr His Glu Tyr Ile Phe Gln Gln Val Glu Ser Gln Lys Lys Ala Lys Pro Lys Arg Tyr Phe Thr Ala Cys Gln Gln Ile

Trp Asn Ser Val 435

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2732 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA (ix) FEATURE:

- - (A) NAME/KEY: Coding Sequence (B) LOCATION: 80...1375 (D) OTHER INFORMATION: VR10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

		CATO	AA E	AA E	CTC	TG	r GC1	TTC	ACT	TA 1	TC	AACTCC A TTT The	60 112
											GCA Ala		160
	 										TTG Leu		208
											GAA Glu		256
											GAA Glu		304
											AAG Lys 90		352
											GGT Gly		400
											CAA Gln		448
											GAT Asp		496
											Lys La		544
											AAT Asn 170		592

																_
			GAC Asp 175													640
			CAT His													688
AGA Arg	TGG Trp 205	ACT Thr	TGG Trp	ATA Ile	GGA Gly	CTG Leu 210	GTC Val	ATC Ile	TCA Ser	GAT Asp	GAT Asp 215	GAC Asp	CAG Gln	GGT Gly	ATT Ile	736
CAG Gln 220	TTT Phe	CTC Leu	TCA Ser	GAT Asp	TTA Leu 225	AGA Arg	GAA Glu	GAA Glu	AGC Ser	CAA Gln 230	AGG Arg	CAT His	GGG Gly	ATC Ile	TGT Cys 235	784
TTA Leu	GCT Ala	TTT Phe	GTT Val	AAT Asn 240	ATG Met	ATC Ile	CCA Pro	GAA Glu	AAC Asn 245	ATG Met	CAG Gln	ATA Ile	TAC Tyr	ATG Met 250	ACA Thr	832
AGG	GCT Ala	ACA Thr	ATA Ile 255	TAT Tyr	GAT Asp	AAA Lys	CAA Gln	ATT Ile 260	ATG Met	ACA Thr	TCT Ser	TCA Ser	GCA Ala 265	AAG Lys	GTT Val	880
GTT Val	ATC Ile	ATT Ile 270	TAT Tyr	GGT Gly	GAA Glu	ATG Met	AAC Asn 275	TCT Ser	ACT Thr	CTA Leu	GAA Glu	GTA Val 280	AGC Ser	TTC Phe	AGA Arg	928
AGA Arg	TGG Trp 285	GAA Glu	GAT Asp	TTA Leu	GGT Gly	GCT Ala 290	CGG Arg	AGA Arg	ATC Ile	TGG Trp	ATC Ile 295	ACA Thr	ACC Thr	TCA Ser	CAA Gln	976
			ATA Ile													1024
GGC Gly	CCT Pro	ATC Ile	ACT Thr	TTT Phe 320	GCA Ala	CAC His	CAC His	AAA Lys	GTT Val 325	GAG Glu	ATT Ile	CCT Pro	AAA Lys	TTA Leu 330	AGG Arg	1072
			CAA Gln 335													1120
CAT His	ACT Thr	ATA Ile 350	CTG Leu	GAG Glu	TGG Trp	TAA Asn	TAT Tyr 355	TTT Phe	AAT Asn	TGT Cys	TCA Ser	ATC Ile 360	TCT Ser	AAG Lys	AAC Asn	1168
			ATG Met													1216
			AAC Asn													1264
TAT Tyr	AAT Asn	GCT Ala	GTT Val	TAT Tyr 400	GTT Val	GCG Ala	GCC Ala	CAC His	ACC Thr 405	TAC Tyr	CAT His	GAA Glu	CAC His	ATT Ile 410	CTT Leu	1312
			GAG Glu 415													1360
GTT	TGT	CAG	CAG	ATA	TAG	AACA	STG 7	rgtgi	TAAA	GT C	CAGA'	rgati	A AG	ratgo	CCAA .C	1416

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Val Cys Gln Gln Ile 430

ATAGAACAAA CCTACTGCCT CTCAAGAGCT GTATCATTTC TGGCTTTTGA AGAACCACTG 1476 GGGATGGCTC TAGGCTGCAT GGCACTATCC TTCTCGGCCA TCACAATTCT AGTACTAGTC 1536 ACATTTGTGA AGTACAAGAA TACTCCCATT GTGAAGGCCA ATAACCGCAT TCTCAGCTAC 1596 ATCCTGCTCA TCTCTCTAGT CTTCTGTTTT CTCTGCTCCC TGCTCTTCAT TGGACATCCT 1656 GACCAGGTCA CCTGCATCTT GCAGCAGACC ACATTTGGAG TATTTTTCAC TGTGTCTGTT TCTACAGTGT TGGCCAAAAC AATAACTGTG GTCATGGCTT TCAAGTTCAC TACTCCAGGA 1776 AGAAGGATGA GAGGGATGTT GGTAACAGGT GCACCTAAGT TGGTCATTCC CATTTGTACC CTAATCCAAC TTGTTCTCTG TGGAATCTGG TTGGTAACAT CTCCTCCATT TATTGACAGA 1896 GATATACAAT CTGAACATGG GAAGGTAGTC ATTCTTTGCA ATAAAGGCTC TGTCATTGCC TTCCACATTG TCCTGGGATA CTTGGGCTCC TTGGCTCTGG GGAGCTTCAC TTTGGCTTTC 2016 TTGGCTAGGA ACCTTCCTGA CACATTCAAT GAAGCCAAAT TCCTAACTTT CAGCATGCTG 2076 GTGTTCTGCA GTGTCTGGAT CACCTTCCTC CCTGTCTACC ACAGCACCAG GGGGAAGGTC 2136 ATGGTGGTTG TGGAGGTTTT CTCAATCTTG GCTTCTAGTG CAGGGTTGCT AATGTGTATC TTTGTCCCAA AGTGTTATGT TATTTTAGTT AGACCAGATT CAAATTTTAC AAAGAACCGC 2256 AAAGGTAAAT TGCTTTATTG AAATTTTCAT GGTATGAAAA TGTTAGATTA TATTCAACTT 2316 ATCTTATTCT TCATCTTAAC AAAAGTAGTA CTTCATCATA TAAAAAATTA AGTAATATAC 2376 AGATTTATAC TTACAAACTG GACAGCAAAC ATGAATATGT TTAGAACTGG GAATCTCAAT 2436 TGAGGAATGG GTATCATCAT TTTGACCTGT GGTTATGTGT TTAAGCCATG TGTTTAATTA 2496 ATGATTAACA TGAGGTTGCC CTACTGTCTG TGAACCATAC CACCTCTAGG CACACTGTCC 2556 TTGAGTTATA AGATAGGGTA CTGCATACAA AATGGACATG AAACCAGTAA TCAACATTAT CCCTCTTGCT TTCATGGAGT TCTTGCATCC AATTTCATGC CTTGACTTCA TTCAATGTAC 2676

(2) INFORMATION FOR SEQ ID NO:20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 432 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Phe Leu Ser Leu Lys Phe 10 Ser Leu Ile Leu Cys Cys Leu Thr Glu Ala Ser Cys Phe Trp Arg Ile 20 25 Lys Asn Ser Glu Asp Ser Asp Gly Asp Leu Gln Arg Glu Cys His Phe 35 40 45 Tyr Leu Trp Val Ile Asp Lys Pro Ile Glu Asp Asn Phe Tyr Asn Ser 55 Val Leu Asn Phe Arg Ile Ser Ala Ser Glu Tyr Glu Phe Leu Leu Val 70 Met Phe Phe Ala Thr Asp Glu Ile Asn Lys Asn Pro Tyr Leu Leu Pro 90 Asn Ile Thr Leu Ile Phe Ser Ile Val Gly Gly His Cys His Asp Leu 100 105 Leu Arg Gly Leu Asp Gln Ser Tyr Thr Gln Ile Asn Gly Arg Val Asn 115 120 125 120 Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Asn Ile Gly Leu 130 135 140 Thr Gly Pro Ser Trp Lys Lys Ser Leu Lys Leu Ala Met Asp Ser Ser 150 155 Ile Pro Met Val Phe Phe Gly Pro Phe Asn Pro Asn Leu Arg Asp His 170 175 165 Asp Arg Leu Pro His Val His Gln Val Ala Pro Lys Asp Thr His Leu 180 185 190 Ser His Gly Met Val Ser Leu Met Phe His Phe Arg Trp Thr Trp Ile · 195 200 205

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Gly Leu Val Ile Ser Asp Asp Gln Gly Ile Gln Phe Leu Ser Asp 215 220 Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn 225 230 235 Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr 250 245 Asp Lys Gln Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly 265 260 270 Glu Met Asn Ser Thr Leu Glu Val Ser Phe Arg Arg Trp Glu Asp Leu 275 280 285 Gly Ala Arg Arg Ile Trp Ile Thr Thr Ser Gln Trp Asp Ile Ile Leu 295 300 Asn Lys Lys Glu Phe Thr Leu Asn Leu Phe His Gly Pro Ile Thr Phe 310 315 Ala His His Lys Val Glu Ile Pro Lys Leu Arg Asn Phe Met Gln Thr 325 330 Met Asn Thr Ala Lys Tyr Pro Val Asp Ile Ser His Thr Ile Leu Glu 340 345 Trp Asn Tyr Phe Asn Cys Ser Ile Ser Lys Asn Ser Ser Lys Met Asp 360 365 Leu Phe Thr Ser Asn Asn Thr Leu Glu Trp Thr Ala Leu His Asn Tyr 375 380 Asp Met Ala Met Ser Asp Glu Gly Tyr Asn Leu Tyr Asn Ala Val Tyr 390 395 Val Ala Ala His Thr Tyr His Glu His Ile Leu Gln Gln Val Glu Ser 405 410 415 Gln Lys Lys Val Glu His Asn Arg Tyr Phe Thr Val Cys Gln Gln Ile 420 -425 430

(2) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2962 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 81...1601
 - (D) OTHER INFORMATION: VR11

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

					C F	TG P	AG A	AAG (CTC :	rgt (GCT T	GGAT FTC 1 Phe 1	ACT I	ATT Ile			60 L10
												TTG Leu		_		1	L58
				-								GAT Asp				2	206
															GAA Glu	2	254
GAT	AAT	TTT	TAT	AAT	TCA	GTT	TTA	AAT	TTT	AGA	ATA	TCA	GCA	AGT	GAA .	:	302

																•
Asp	Asn 60	Phe	Tyr	Asn	Ser	Val 65	Leu	Asn	Phe	Arg	Ile 70	Ser	Ala	Ser	Glu	
				CTG Leu												350
				TTA Leu 95												398
				GAT Asp												446
				GTG Val												494
				GGC Gly												542
				TCT Ser												590
				GAC Asp 175												638
CCC Pro	AAG Lys	GĄC Asp	ACA Thr 190	CAT His	TTA Leu	TCC Ser	CAT His	GGC Gly 195	ATG Met	GTC Val	TCC Ser	TTG Leu	ATG Met 200	TTT Phe	CAT His	686
TTT Phe	AGA Arg	TGG Trp 205	ACT Thr	TGG Trp	ATA Ile	GGA Gly	CTG Leu 210	GTC Val	ATC Ile	TCA Ser	GAT Asp	GAT Asp 215	GAC Asp	CAG Gln	GGT Gly	734
ATT Ile	CAG Gln 220	TTT Phe	CTC Leu	TCA Ser	GAT Asp	TTA Leu 225	AGA Arg	GAA Glu	GAA Glu	AGC Ser	CAA Gln 230	AGG Arg	CAT His	GGG Gly	ATC Ile	782
				GTT Val												830
				ATA Ile 255												878
GTT Val	GTT Val	ATC Ile	ATT Ile 270	TAT Tyr	GGT Gly	GAA Glu	ATG Met	AAC Asn 275	TCT Ser	ACT Thr	CTA Leu	GAA Glu	GTA Val 280	AGC Ser	TTC Phe	926
AGA Arg	AGA Arg	TGG Trp 285	GAA Glu	GAT Asp	TTA Leu	GGT Gly	GCT Ala 290	CGG Arg	AGA Arg	ATC Ile	TGG Trp	ATC Ile 295	ACA Thr	ACC Thr	TCA Ser	974
			_	ATA Ile												1022
				ACT Thr											TTA Leu	1070

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315					320					325					330	
														GAT Asp 345		1118
														TCT Ser		1166
														GAA Glu		1214
														TAC Tyr		1262
														CAC His		1310
														TAT Tyr 425		1358
														TTT Phe		1406
														CAG Gln		1454
														CTT Leu		1502
														AGT Ser		1550
			-											ACA Thr 505		1598
ATA Ile	TAG	AACA	GTG :	rgtg	AAAT	GT C	CAGA'	TGAT.	A AG	TATG	CCAA	CAT	AGAA	CAA 2	ACCTAC	1657
TGC	CTCT	CAA (GAGC'	TGTA:	TC A	rttc'	TGGC'	T TT	TGAA	GAAC	CAC'	TGGG	GAT (GGCT	CTAGGC	1717
															AAGTAC	1777
															ATCTCT ACCTGC	1837 1897
															TTGGCC	1957
AAA	ACAA'	TAA	CTGT	GGTC	AT G	GCTT	TCAA	G TT	CACT	ACTC	CAG	GAAG	AAG	GATG.	AGAGGG	2017
															CTTGTT TCTGAA	2077 2137
															GTCCTG	2137
GGA'	TACT'	TGG	GCTC	CTTG	GC T	CTGG	GGAG	C TT	CACT	TTGG	CTT	TCTT	GGC	TAGG.	AACCTT	2257
															AGTGTC GTGGAG	2317 2377
															AAGTGT	2437
TAT	GTTA'	TTT	TAGT	TAGA	CC A	GATT	CAAA	T TT	TACA	AAGA	ACC	GCAA	AGG	TAAA	TTGCTT	2497
TAT'	TGAA	ATT	TTCA	TGGT	AT G	AAAA	TGTT.	A GA	TTAT.	ATTC	AAC	TTAT	CTT	ATTC	TTCATC	2557

TTAACAAAAG	TAGTACTTCA	TCATATAAAA	AATTAAGTAA	TATACAGATT	TATACTTACA	2617
AACTGGACAG	CAAACATGAA	TATGTTTAGA	ACTGGGAATC	TCAATTGAGG	AATGGGTATC	2677
ATCATTTTGA	CCTGTGGTTA	TGTGTTTAAG	CCATGTGTTT	AATTAATGAT	TAACATGAGG	2737
TTGCCCTACT	GTCTGTGAAC	CATACCACCT	CTAGGCACAC	TGTCCTTGAG	TTATAAGATA	2797
GGGTACTGCA	TACAAAATGG	ACATGAAACC	AGTAATCAAC	ATTATCCCTC	TTGCTTTCAT	2857
GGAGTTCTTG	CATCCAATTT	CATGCCTTGA	CTTCATTCAA	TGTACTATGA	CAAAGGTACA	2917
TAAATAAATA	AACACTTTCC	CCACAAAAAA	ааааааааа	AAAAA		2962

(2) INFORMATION FOR SEQ ID NO:22:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 507 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Met Lys Lys Leu Cys Ala Phe Thr Ile Ser Phe Leu Ser Leu Lys Phe 10 Ser Leu Ile Leu Cys Cys Leu Thr Glu Ala Ser Cys Phe Trp Arg Ile 20 25 Lys Asn Ser Glu Asp Ser Asp Gly Asp Leu Gln Arg Glu Cys His Phe 40 35 Tyr Leu Trp Val Ile Asp Lys Pro Ile Glu Asp Asn Phe Tyr Asn Ser 55 60 Val Leu Asn Phe Arg Ile Ser Ala Ser Glu Tyr Glu Phe Leu Leu Val 75 70 Met Phe Phe Ala Thr Asp Glu Ile Asn Lys Asn Pro Tyr Leu Leu Pro 90 Asn Ile Thr Leu Ile Phe Ser Ile Val Gly Gly His Cys His Asp Leu 100 105 110 Leu Arg Gly Leu Asp Gln Ser Tyr Thr Gln Ile Asn Gly Arg Val Asn 120 115 Phe Val Asn Tyr Phe Cys Tyr Leu Asp Asp Ser Cys Asn Ile Gly Leu 135 140 Thr Gly Pro Ser Trp Lys Lys Ser Leu Lys Leu Ala Met Asp Ser Ser 150 155 Ile Pro Met Val Phe Phe Gly Pro Phe Asn Pro Asn Leu Arg Asp His 170 165 Asp Arg Leu Pro His Val His Gln Val Ala Pro Lys Asp Thr His Leu 180 185 Ser His Gly Met Val Ser Leu Met Phe His Phe Arg Trp Thr Trp Ile 200 205 195 Gly Leu Val Ile Ser Asp Asp Asp Gln Gly Ile Gln Phe Leu Ser Asp 220 215 Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn 230 235 Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr 250 245 Asp Lys Gln Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly 265 260 270 Glu Met Asn Ser Thr Leu Glu Val Ser Phe Arg Arg Trp Glu Asp Leu 280 285 Gly Ala Arg Arg Ile Trp Ile Thr Thr Ser Gln Trp Asp Ile Ile Leu 295 300 Asn Lys Lys Glu Phe Thr Leu Asn Leu Phe His Gly Pro Ile Thr Phe 310 315 Ala His His Lys Val Glu Ile Pro Lys Leu Arg Asn Phe Met Gln Thr 330 325 Met Asn Thr Ala Lys Tyr Pro Val Asp Ile Ser His Thr Ile Leu Glu 340

348

Trp Asn Tyr Phe Asn Cys Ser Ile Ser Lys Asn Ser Ser Lys Met Asp 355 360 365 Leu Phe Thr Ser Asn Asn Thr Leu Glu Trp Thr Ala Leu His Asn Tyr 375 380 370 Asp Met Ala Met Ser Asp Glu Gly Tyr Asn Leu Tyr Asn Ala Val Tyr 385 390 395 400 Val Ala Ala His Thr Tyr His Glu His Ile Leu Gln Gln Val Glu Ser 405 410 415 Gln Lys Lys Val Glu His Asn Arg Tyr Phe Thr Val Cys Gln Gln Val 420 425 430 Ser Ser Leu Met Lys Thr Arg Val Phe Thr Asn Pro Val Gly Glu Leu 440 Val Asn Met Lys His Arg Glu Asn Gln Cys Thr Glu Tyr Asp Ile Phe 455 Ile Ile Trp Asn Phe Pro Gln Gly Leu Gly Leu Lys Leu Lys Ile Gly 470 475 Ser Tyr Ile Pro Cys Phe Pro Lys Ser Gln Gln Leu His Ile Ser Asp 485 490 Asp Leu Glu Trp Ala Met Gly Gly Thr Ser Ile 500 505

(2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2821 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 60...992

70

(D) OTHER INFORMATION: VR12

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

60 GACGTTTTTC TGCATCAGAA ACGGATTTCA CAGCAGCTCC ATCTCAGATC CTAGCAGAC A TGA AGC AGC TCT GCA CTT TCA CTA TTT CAT TGT TGT TTC TGA AGT TTT 108 t Lys Gln Leu Cys Thr Phe Thr Ile Ser Leu Leu Phe Leu Lys Phe Se 10 CTC TCA TCT TGT GCT GTT GGA GTG AAC CAA GCT GCT TTT GGA GGA TAA 156 r Leu Ile Leu Cys Cys Trp Ser Glu Pro Ser Cys Phe Trp Arg Ile Ly 20 AGA AGA GTG AAG ATA ATG ATG GAG ATT TAC AAA GGG AGT GTC ATT TTT 204 s Lys Ser Glu Asp Asn Asp Gly Asp Leu Gln Arg Glu Cys His Phe Ty 35 ACC TTT GGA AAA CTG ATG AAC CTA TTG AAG ATA GTT TTT ATA ATT ATG 252 r Leu Trp Lys Thr Asp Glu Pro Ile Glu Asp Ser Phe Tyr Asn Tyr As 60 55 300 ATT TAA GTT TTA GAA TTG CAG GAA GTG AAT ATG AGC TTC TTC TGG TAA p Leu Ser Phe Arg Ile Ala Gly Ser Glu Tyr Glu Leu Leu Leu Val Me

TGT TTT TTG CTA CTG ATG AGA TCA AGA ATC CTT ATC TTT TAC CCA

t Phe Phe Ala Thr Asp Glu Ile Asn Lys Asn Pro Tyr Leu Leu Pro As.

75

85		90	95	
ACA TGA GTT TGA TG n Met Ser Leu Met 100		Gly Gly Asn		
TGA GAA GTC TGG AT u Arg Ser Leu Asp 115				
TTG TTA ATT ATT TC e Val Asn Tyr Phe 130				
CAG GAC CAT CAT GG r Gly Pro Ser Trp 45				r Me
TGC CAC TGG TTT TC t Pro Leu Val Phe 165				
ACC GGC TGC CCC AT p Arg Leu Pro His 180		Ala Pro Lys		
CCC ATG GCA TGG TC r His Gly Met Val 195				
GAC TGG TCA TCT CA y Leu Val Ile Ser 210				
TAA GAG AAG AAA GC u Arg Glu Glu Ser 25				n Me
TGA TCC CAG AAA AC t Ile Pro Glu Asn 245				
ATA CAC AAA TTA TG p Thr Gln Ile Met 260		Lys Val Val		
ACA TGA ACT CTA CT p Met Asn Ser Thr 275				
GTG CTC GGA GAA TO y Ala Arg Arg Ile 290				
ATA AAA AAA GAC TI n Lys Lys Arg Leu 05		CTTC CATGGGA	CTA TTACTTTTGC	ACACC 1027
ACAAAGATGA GATTCCT	AAA TTTAGGAATT	TTATGCAAAC A	AAGAAAACT GCCAA	ATACC 108
TTGTAGATAT TTCTCAT				
ACAGCAGTAA AATGGGT				
ACTATGATAT GGCCCTG				
CCCACACCTA CCATGAA AAAGATATTT CACTGCT				
CAGGATTCAG GAAAATT				

GCCTAGAAAA	TGAGGTTTCC	AATGAAACAG	ATATGGAACA	GTGTGTGAGA	TGTCCAGATA	1507
ATAAATATGC	CAATTTAGAG	CAAACCCACT	GCCTCCAAAG	AACGGTGTCA	TTTCTGGCTT	1567
ATGAAGATCC	ATTGGGGATG	GCTCTAGGCT	GCATGGCACT	GTCCTTCTCG	GCCATCACAA	1627
TTCTAGTCCT	CGTCACATTT	GTGAAGTACA	AGGATACTCC	CATTGTGAAG	GCCAATAACC	1687
GCATTCTCAG	CTACATCCTG	CTCATCTCTC	TCGTCTTCTG	CTTTCTCTGT	TCCCTGCTCT	1747
TCATTGGACA	TCCCGACCAG	GTCACCTGCA	TCTTGCAGCA	GACCACATTT	GGAGTATTGT	1807
TCACTGTGTC	TGTTTCTACA	GTGTTGGCCA	AAACAATAAC	TGTGGTCATG	GCTTTCAAGC	1867
TCACTACTCC	AGGAAGAAGG	ATGAGAGGGA	TGATGATGAC	AGGGGCACCT	AAGTTGGTCA	1927
TTCCCATTTG	TACCCTGATC	CAACTTGTTC	TCTGTGGAAT	CTGGTTGGTC	ACATCTCCTC	1987
CCTTTATTGA	CAGAGATATA	CAATCTGAAC	ATGGGAAGAT	TGTCATTCTT	TGCAATAAAG	2047
GCTCTGTCGT	TGCCTTCCAC	GTCGTCCTGG	GATACTTGGG	CTCCTTGGCT	CTGGGGAGCT	2107
TCACTTTGGC	TTTCTTGGCT	AGGAACCTTC	CTGACACATT	CAATGAAGCC	AAGTTCCTAA	2167
CTTTCAGCAT	GCTGGTGTTC	TGCAGTGTCT	GGATCACCTT	CCTCCCTGTC	TACCACAGCA	2227
CCAGGGGGAA	GGTCATGGTG	GTTGTGGAGG	TTTTCTCCAT	CTTGGCTTCT	AGTGCAGGGT	2287
TGCTAATGTG	TATCTTTGTC	CCAAAGTGTT	ATGTTATTTT	AATTAGACCA	GATTCAAATT	2347
TTATACAGAA	CCACAAAGGT	AAATTGCTTT	ATTGAAACTT	TCATGGTATG	AAAATGTTAG	2407
ATGATATTCA	ACTTATCTTA	TTCTTCATCT	TAATAAAAGC	AGTACTTCAT	CATATAAAAA	2467
ATAAAGTAAT	ATACAGATTT	ATACTTACAA	ACTGGACAGC	AAACATGAAT	ATGTTGAGAA	2527
CTGGGATTCT	CAATTGAGGA	ATGGCTACCA	ATATTTTGAT	CTGTGGTTTT	GTGTTTAAGC	2587
CATGTACTTA	ATTAATGATT	AACATGAGGT	TACCCTACTG	TCTTTGAACA	GCGCCACCTC	2647
TAGGCATGCT	GTCCTTGAGT	TATAAGAAAG	GGTACTGCAT	ACACAATGGA	CATGAAGCCA	2707
GTAATCAACA	TTATTCCACT	TGCTTTCATG	GAGTTCTTAC	TTCCAAGTTC	ATGCCTTGAC	2767
TTTATTCAAT	GTTCTATGAC	AAAGGTAGAA	TAAATAAATA	AACACTTTCC	TCAC	2821

(2) INFORMATION FOR SEQ ID NO:24:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 311 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met 1	Lys	Gln	Leu	Cys 5	Thr	Phe	Thr	Ile	Ser 10	Leu	Leu	Phe	Leu	Lys 15	Phe
Ser	Leu	Ile	Leu 20	Cys	Cys	Trp	Ser	Glu 25	Pro	Ser	Cys	Phe	Trp	Arg	Ile
Lys	Lys	Ser 35	Glu	Asp	Asn	Asp	Gly 40	Asp	Leu	Gln	Arg	Glu 45	Cys	His	Phe
Tyr	Leu 50	Trp	Lys	Thr	Asp	Glu 55	Pro	Ile	Glu	Asp	Ser 60	Phe	Tyr	Asn	Tyr
Asp 65	Leu	Ser	Phe	Arg	Ile 70	Ala	Gly	Ser	Glu	Tyr 75	Glu	Leu	Leu	Leu	Val 80
Met	Phe	Phe	Ala	Thr 85	Asp	Glu	Ile	Asn	Lys 90	Asn	Pro	Tyr	Leu	Leu 95	Pro
Asn	Met	Ser	Leu 100	Met	Phe	Ser	Ile	Ile 105	Gly	Gly	Asn	Сув	His 110	Asp	Leu
Leu	Arg	Ser 115	Leu	Asp	Gln	Glu	Tyr 120	Ala	Gln	Ile	Asp	Gly 125	His	Met	Asn
Phe	Val 130	Asn	Tyr	Phe	Cys	Tyr 135	Leu	Asp	Asp	Ser	Cys 140	Ala	Thr	Gly	Leu
Thr 145	Gly	Pro	Ser	Trp	Lys 150	Thr	Ser	Leu	Lys	Leu 155	Ala	Met	His	Ser	Ser 160
Met	Pro	Leu	Val	Phe 165	Phe	Gly	Pro	Phe	Asn 170	Pro	Asn	Leu	Arg	Asp 175	His
Asp	Arg	Leu	Pro 180	His	Val	His	Gln	Val 185	Ala	Pro	Lys	Asp	Thr 190	His	Leu
Ser	His	Gly 195	Met	Val	Ser	Leu	Met 200	Phe	His	Phe	Arg	Trp 205	Thr	Trp.	Ile
Gly	Leu 210	Val	Ile	Ser	Asp	Asp 215	Asp	Gln	Gly	Ile	Gln 220	Phe	Leu	Ser	Asp

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Leu Arg Glu Glu Ser Gln Arg His Gly Ile Cys Leu Ala Phe Val Asn 230 235 Met Ile Pro Glu Asn Met Gln Ile Tyr Met Thr Arg Ala Thr Ile Tyr · 245 250 Asp Thr Gln Ile Met Thr Ser Ser Ala Lys Val Val Ile Ile Tyr Gly 260 265 270 Asp Met Asn Ser Thr Leu Glu Ala Ser Phe Arg Arg Trp Glu Glu Leu 280 285 Gly Ala Arg Arg Ile Trp Ile Thr Thr Thr Gln Trp Asp Val Ile Thr 295 300 Asn Lys Lys Arg Leu His Pro 305

(2) INFORMATION FOR SEQ ID NO:25:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2773 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence (B) LOCATION: 3...1238

 - (D) OTHER INFORMATION: VR13

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

	AGT Ser							Asp		47
	CAA Gln									95
									GCA Ala	143
	TAT Tyr 50									191
	AAT Asn								ATC Ile	239
	GGA Gly									287
	ATA Ile		His			Asr				335
		Ala			Gly			Thr	TCC Ser	383
									TCA	431

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	130			135				140			
TTT AAT Phe Asn 145										479	
GTA GCC Val Ala 160										527	
TTT CAT Phe His										575	
AAG GGT Lys Gly	Ile									623	
GGG ATC Gly Ile										671	
TAC ATG Tyr Met 225										719	
GCA AAA Ala Lys 240										767	
AGC TTT Ser Phe										815	
ACC TCA Thr Ser										863	
CTC TTC Leu Phe										911	
AAA TTT Lys Phe 305										959	
GAT ATT Asp Ile 320		•	 	 	_	_	_	 _	 _	 1007	
TCT AAG Ser Lys										1055	
GAA TGG Glu Trp										1103	
TAC AAT Tyr Asn										1151	
CAT ATT His Ile 385	Phe									1199)

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TTT TTC ACT GTT TGT CAG CAG CAG ATA TGG AAC AGT GTG TGAAGTGTCC AT 1250 Phe Phe Thr Val Cys Gln Gln Gln Ile Trp Asn Ser Val

ATGATAAGTA TGCCAACATA GAGAAAACCC ACTGCCTCTC AAGAGCTGTA TCATTTCTGG CTTATGAAGA TCCATTGGGG ATAGCTCTAG GCTGCATAGC ACTGTCCTTC TCAGCCATCA CAATTCTAGT ACTAATCACA TTTTTGAAGT ACAAGGATAC TCCCATTGTG AAGGCCAATA 1430 ACCGCATTCT CAGCTACATC CTGCTCATCT CTCTAGTCTT CTGCTTTCTC TGCTCCCTGC 1490 TCTTCATTGG ACATCCAAAC CAGGTCTCCT GCGTCTTGCA GCAGACCACA TTTGGAGTAT 1550 TTTTCACTGT GTCTGTTTCT ACAGTGTTGG CCAAAACAAT AACTGTGGTC ATGGCTTTCA AGCTCACTAC TCCAGGAAGA AGAATGAGAG AGATGTTGGT AACAGGGGCA CCTAAGTTGG 1670 TCATTCCCAT TTGTACCCTA ATCCAATTTG TTCTCTGTGG AATCTGGTTG ATAACATCTC 1730 CTCCATTTAT TGACAGAGAT ATACAATCTG AGCATGGGAA GATTGTCATT CTTTGCAATA AAGGCTCTGT CATTGCCTTC CATGTTGTCC TGGGATACTT GGGCTCCTTG GCTCTGGGGA 1850 GCTTCACTTT GGCTTTCTTG GCTAGGAACC TTCCTGACAC ATTCAATGAA GCCAAATTCC TGACTTTCAG CATGCTGGTG TTCTGCAGTG TCTGGATCAC CTTTCTCCCT GTCTACCATA 1970 GCACCAGGGG GAAGGTCATG GTGGTTGTGG AGGTTTTCTC AATCTTGGCT TCTAGTGCAG 2030 2090 ATTTTATACG GAAGTACAAA GATAAATTTC GTTATTGAAA TATTCATACT ATGAAAATGT TAGATTATAC TCAACATATT TTTCTTTGTC TTAACAAAAG TAGTACTTAA TCTTATAAAA 2210 ATTTAAATAA TATACAAATT TGAACTTACA AACAGGACAG AACTGTCTAT TGTAATACCA 2270 ATTACAAAAC TTTGGTGAAA AATGGTCTCA TTCATAAGGA CACAATTCTG AAGATATTGA 2330 GAACCAGGAA TCTCAACTGC GGAAACGCTA CCATCATCCT GACCTGTGGT TTTGTGTGTA AAGCATGAAC TTAATTAATG ATTAATATAA GGTGACCATA CTGACTGTGA ACACTACCAT 2450 CTCTGGGCAA GTTGTTCTTG TAGTTGTAAG AAAAAGCTCT GAAGACAACA TGGAAGTAAA GCCAGTAATC ACCATTATCC CTCATGCTTT CATGGAGTGG CTGCATCCAA TTTCATGCCT 2510 2570 TGGCTTCATT CAATATACTG TGACCAAGGT ACATAAGTAA AGAAACACTT TTCTTACAAG 2630 GTATTTTTAC ATCAACGGAA TTTAAAATAT CAACAAAATG GTAAATTGTT TCTGTTGAGA 2750 TTTAGAATAT CATCGATTCC TGA

(2) INFORMATION FOR SEQ ID NO:26:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 412 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Ala Ser Cys Phe Trp Arg Ile Lys Asn Ser Glu Asp Asn Asp Gly Asp 10 Leu Gln Arg Glu Cys His Phe Tyr Leu Gly Ala Val Asp Lys Pro Ile 25 30 Glu Asp Asn Phe Tyr Asn Ser Leu Leu Lys Phe Arg Ile Ala Ala Ser 35 40 Glu Tyr Glu Phe Leu Leu Val Met Phe Phe Ala Thr Asp Glu Ile Asn 55 60 Lys Asn Pro Tyr Leu Leu Pro Asn Ile Thr Leu Met Phe Ser Ile Ile 70 75 Gly Gly Asn Cys His Asp Leu Leu Arg Gly Leu Asp Gln Ala Tyr Thr 90 85 Gln Ile Asn Gly His Met Asn Phe Val Asn Tyr Phe Cys Tyr Leu Asp 100 105 Asp Ser Cys Ala Ile Gly Leu Thr Gly Pro Ser Trp Lys Thr Ser Leu 120 125 Lys Leu Ala Met His Ser Ser Met Pro Leu Val Phe Phe Gly Ser Phe 135 Asn Pro Asn Leu His Asp His Asp Arg Leu His His Val His Gln Val 150 155 Ala Thr Lys Asp Thr His Leu Ser His Gly Ile Val Ser Leu Met Phe .

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170 His Phe Arg Trp Thr Trp Ile Gly Leu Val Ile Ser Asp Asp Asp Lys 185 180 Gly Ile Gln Phe Leu Ser Asp Leu Arg Glu Glu Ser Gln Arg His Gly 195 200 205 Ile Cys Leu Ala Phe Val Asn Met Ile Pro Glu Asn Met Gln Ile Tyr 210 215 220 Met Thr Arg Ala Thr Ile Tyr Asp Lys Gln Ile Met Thr Ser Leu Ala 230 235 Lys Val Val Ile Ile Tyr Gly Glu Met Asn Ser Thr Leu Glu Val Ser 245 250 255 Phe Arg Arg Trp Glu Asn Leu Gly Ala Arg Arg Ile Trp Ile Thr Thr 260 265 270 Ser Gln Trp Asp Val Ile Thr Asn Lys Lys Glu Phe Thr Leu Asn Leu 280 275 285 Phe His Gly Thr Ile Thr Phe Ala His Arg Arg Phe Glu Ile Pro Lys 290 295 300 Phe Lys Lys Phe Met Gln Thr Met Asn Thr Ala Lys Tyr Pro Val Asp 310 315 Ile Ser His Thr Ile Leu Glu Trp Asn Tyr Phe Asn Cys Ser Ile Ser 325 330 335 Lys Asn Ser Ser Lys Met Asp His Ile Thr Phe Asn Asn Thr Leu Glu 340 345 Trp Thr Ala Leu His Asn Tyr Asp Met Val Met Ser Asp Glu Gly Tyr 355 360 365 Asn Leu Tyr Asn Ala Val Tyr Ala Val Ala His Thr Tyr His Glu His 375 380 Ile Phe Gln Gln Val Glu Ser Gln Lys Lys Ala Lys Pro Lys Arg Phe 390 395 Phe Thr Val Cys Gln Gln Gln Ile Trp Asn Ser Val

(2) INFORMATION FOR SEQ ID NO:27:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3108 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 116...2527
 - (D) OTHER INFORMATION: VR14

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

								SATGTG S ATG Met 1	60 118
 	CTC Leu		166						
 	GAT Asp		214						
 	GCA Ala		262						

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35			40			45			
				GAT Asp					310
				AAA Lys					358
				CCT Pro					406
				CGT Arg 105			_		 454
				AAA Lys					502
				TGT Cys					550
 	 			TGG Trp		 		 	598
				TAT Tyr					646
				CTC Leu 185					694
				TCC Ser					742
				GAT Asp					790
				GAA Glu					838
				GAT Asp				Thr	886
				ATG Met 265					934
				ATT Ile					982
				TGG Trp					1030

								- 1	117-							-
			AAA Lys													1078
			CCC Pro 325													1126
			TTC Phe													1174
			TAC Tyr													1222
			TAA Asn													1270
			ATG Met													1318
			ATA Ile 405													1366
			GCA Ala													1414
Cys	Leu 435	Lys	Val	Asn	Ser	Phe 440	Leu	Arg	Arg	Ile	Tyr 445	Phe	Thr	Asn		1462
CCT Pro 450	GGG Gly	Asp	AAA Lys	GTG Val	TTT Phe 455	ATG Met	AAG Lys	CAA Gln	AGA Arg	GTA Val 460	ATA Ile	ATG Met	CAC His	GAT Asp	GAA Glu 465	1510
			GTT Val												AAG Lys	1558
			GGA Gly 485				Pro		Leu							1606
			GTA Val												ATG Met	1654
															TTA Leu	1702
	Lys														CCT Pro 545	1750
					Asn										GTG Val	1798
AAG	CAT	CAT	GAC	ACT	CCT	ATT	GTG	AAG	GCC	TAA	AAC	AGA	AGC	CTC	AGC	. 1846

																-
Lys	His	His	Asp 565	Thr	Pro	Ile	Val	Lys 570	Ala	Asn	Asn	Arg	Ser 575	Leu	Ser	
		TTA Leu 580														1894
		GGC Gly														1942
		ATT Ile														1990
		GTG Val														2038
		TTC Phe														2086
		CTC Leu 660				Leu										2134
		GTT Val														2182
		AAC Asn														2230
		TGC Cys														2278
		CCT Pro														2326
		TTC Phe 740														2374
		GGC Gly													GCA Ala	2422
		GCT Ala														2470
		ATG Met														2518
		TTC Phe		ACAA	ATA :	rtta(ggaa'	TT C	rgtc	AAAT(G TA	aagt'	rggt	ACA!	FACCCA	2576
															GCTCTA PTGTAC	2636 2696

	TCATTCACTT	TCTTCATTTT	CTCTCAGAGA	ACTAAACTCT	CTAATTATTA	CAATTTTATT	2756
	CTTCATTTTG	CTTTCATGGA	GATTGCCCTC	TGGTAACTTC	CAAAAAATGT	TGATAAGGCA	2816
	GTTGAATCCA	CCACTTTGTG	TAGAAAAATG	AGATCTAGGA	AGACAGGGTT	ACACATAAAA	2876
	ACCATCTACC	AAAATAAATA	ATCAATGAGA	AACACAGACT	AACTAAATAA	TCAGCAAAGA	2936
•	TGAAATCAGA	ACATATTTTC	TAATTTCCAG	TAAGAGCACA	CACATAAGAA	AATACTTACT	2996
	TTTTTCATCT	GTTCTTCAAT	CTACTGGCCA	ATAGTCTAAG	GAGGAAATGT	TCCTTTTCTG	3056
	CTGTCAAATA	TTATATAAAA	ATATCCAAAA	AAAAAAAAA	ааааааааа	AA	3108

(2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 804 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Phe Ile Phe Met Glu Val Phe Phe Leu Leu Asn Ile Thr Leu Leu 5 10 Met Ala Asn Phe Ile Asp Pro Arg Cys Phe Trp Arg Ile Asn Leu Asp 20 25 Glu Ile Met Asp Glu Tyr Leu Gly Leu Ser Cys Ala Phe Ile Leu Ala 40 45 Ala Val Gln Thr Pro Ile Glu Asn Asp Tyr Phe Asn Lys Thr Leu Asn 55 60 Val Leu Lys Thr Thr Lys Asn His Lys Tyr Ala Leu Ala Leu Val Phe 70 75 Ala Met Asp Glu Ile Asn Arg Asn Pro Asp Leu Leu Pro Asn Met Ser 90 Leu Ile Ile Arg Tyr Thr Leu Gly Arg Cys Asp Gly Lys Thr Val Ile 100 105 Pro Thr Pro Tyr Leu Phe Arg Lys Lys Glu Ser Pro Ile Pro Asn 120 115 Tyr Phe Cys Asn Glu Glu Thr Met Cys Ser Tyr Leu Leu Thr Gly Pro 135 140 His Trp Glu Val Ser Leu Gly Phe Trp Lys His Met Asn Ser Phe Leu 150 155 Ser Pro Arg Ile Leu Gln Leu Thr Tyr Gly Pro Phe His Ser Ile Phe 170 175 165 Ser Asp Asp Glu Gln Tyr Pro Tyr Leu Tyr Gln Met Ala Pro Lys Asp 185 190 180 Thr Ser Leu Ala Leu Ala Met Val Ser Phe Ile Leu Tyr Phe Ser Trp 205 195 200 Asn Trp Ile Gly Leu Val Ile Pro Asp Asp Gln Gly Asn Gln Phe 215 220 210 Leu Leu Glu Leu Lys Lys Gln Ser Glu Asn Lys Glu Ile Cys Phe Ala 230 235 Phe Val Lys Met Ile Ser Val Asp Asp Val Ser Phe Pro Gln Asn Thr 250 245 Glu Met Tyr Tyr Asn Gln Ile Val Met Ser Ser Thr Asn Val Ile Ile 260 265 270 Ile Tyr Gly Glu Thr Tyr Asn Phe Ile Asp Leu Ile Phe Arg Met Trp 275 280 Glu Pro Pro Ile Leu Gln Arg Ile Trp Ile Thr Thr Lys Gln Leu Asn 295 300 Phe Pro Thr Arg Lys Lys Asp Ile Ser His Gly Thr Phe Tyr Gly Ser 310 315 Leu Thr Phe Leu Pro His His Gly Val Ile Ser Gly Phe Lys Asn Phe 325 330 Val Gln Thr Trp Phe His Leu Arg Asn Thr Asp Leu Tyr Leu Val Met 340 345

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Gln Glu Trp Lys Tyr Phe Asn Tyr Glu Asp Ser Ala Ser Thr Cys Lys Ile Leu Lys Asn Asn Ser Ser Asn Ala Ser Phe Asp Trp Leu Met Glu Gln Lys Phe Asp Met Thr Phe Ser Glu Asn Ser His Asn Ile Tyr Asn Ala Val His Ala Ile Ala His Ala Leu His Glu Met Asn Leu Gln Gln Ala Asp Asn Gln Ala Ile Asp Asn Gly Lys Lys Glu Pro Ser Ser Ser His Cys Leu Lys Val Asn Ser Phe Leu Arg Arg Ile Tyr Phe Thr Asn Pro Pro Gly Asp Lys Val Phe Met Lys Gln Arg Val Ile Met His Asp Glu Tyr Asp Ile Val His Phe Val Asn Leu Ser Gln His Leu Gly Ile Lys Met Lys Leu Gly Lys Phe Ser Pro Tyr Leu Pro His Gly Arg His Ser His Leu Tyr Val Asp Arg Ile Glu Leu Ala Thr Gly Arg Arg Lys Met Pro Ser Ser Val Cys Ser Ala Asp Cys Ser Pro Gly Phe Arg Arg Leu Trp Lys Glu Gly Met Ala Ala Cys Cys Phe Val Cys Ser Pro Cys Pro Glu Asn Glu Ile Ser Asn Glu Thr Thr Val Val Leu Cys Val Phe Val Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ser Leu Ser Tyr Leu Leu Met Ser Leu Met Ser Cys Phe Leu Cys Ser Phe Phe Phe Ile Gly Leu Pro Asn Arg Ala Ile Cys Val Leu Gln Gln Ile Thr Phe Gly Ile Val Phe Thr Met Ala Val Ser Thr Val Leu Ala Lys Thr Val Thr Val Val Leu Ala Phe Lys Val Thr Asp Pro Gly Arg Arg Leu Arg Asn Phe Leu Val Ser Gly Thr Pro Asn Tyr Ile Ile Pro Ile Cys Ser Leu Leu Gln Cys Val Leu Cys Ala Ile Trp Leu Ala Val Ser Pro Pro Phe Val Asp Ile Asp Glu His Thr Leu His Gly His Ile Ile Ile Val Cys Asn Lys Gly Ser Val Thr Ala Phe Tyr Cys Ile Leu Gly Tyr Leu Ala Cys Leu Ala Leu Gly Asn Phe Ser Val Ala Phe Leu Ala Lys Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu Val Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys His Met Val Ala Val Glu Ile Phe Ser Ile Leu Ala Ser Ser Ala Gly Ile Leu Gly Cys Ile Phe Val Pro Lys Ile Tyr Ile Ile Leu Met Arg Pro Glu Arg Asn Ser Thr Gln Lys Ile Arg Glu Lys Ser Tyr Phe

(2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3689 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 39...419

(D) OTHER INFORMATION: VR15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:	
TCAAAATCCG CACTGCCCAA GTTTAAGGCA GGAAAAAT ATG TTC ATT TTC ATG GGA Met Phe Ile Phe Met Gly 1 5	56
GTC TTC TTC CTC CTT AAT ATT ACA CTT CTC ATG GCC AAT TTC ATT AAT Val Phe Phe Leu Leu Asn Ile Thr Leu Leu Met Ala Asn Phe Ile Asn 10 15 20	104
CCC AGG TGC TTT TGG AGA ATA AAT TTG GAT GAA ATA ACG GAT GAA TAT Pro Arg Cys Phe Trp Arg Ile Asn Leu Asp Glu Ile Thr Asp Glu Tyr 25 30 35	152
TTG GGA TTA TCT TGT ACT TTC ATC CTG GCG GCA GTT CAG ACA CCC ACT Leu Gly Leu Ser Cys Thr Phe Ile Leu Ala Ala Val Gln Thr Pro Thr 40 45 50	200
GAA AAA GAT TAT TTC AAC AAG ACT CTT AAT GTT CTA AAA ACA ACT AAA Glu Lys Asp Tyr Phe Asn Lys Thr Leu Asn Val Leu Lys Thr Thr Lys 55 60 70	248
AAC CAC AAA TAT GCT TTG GCA TTG GTG TTT GCA ATG GAT GAA ATC AAC Asn His Lys Tyr Ala Leu Ala Leu Val Phe Ala Met Asp Glu Ile Asn 75 80 85	296
AGA AAT CCT GAT CTT TTA CCA AAT ATG TCT TTG ATT ATA AGA TAC ACT Arg Asn Pro Asp Leu Leu Pro Asn Met Ser Leu Ile Ile Arg Tyr Thr 90 95 100	344
TTG GGC CTT TGT GAT GGA AAA ACT GTA ACA CCT ACA CCA TAT TTA TTT Leu Gly Leu Cys Asp Gly Lys Thr Val Thr Pro Thr Pro Tyr Leu Phe 105 110 115	392
CAT AAA AAA AAA ACA AAG CCC TAT CCC TAATTATTTC TGTAATGAAG AGACTAT His Lys Lys Lys Thr Lys Pro Tyr Pro 120 125	446
TGTACAGACA TGGTTCCATG TCAGAAACAC AGATTTATAT TTAGTAATGC CAGAGTGGAA CTATTTTAAC TATGTAAGCT CAGCATCCAA TTGTAAAATA CTGAAGAACA ATTCATCTGA TGCCTCATTT GATTGGCTAA TGGAACAGAA GTTTGACATG ACCTTTAGTG AGAATAGTCA	566 626 686 746 806 866 926 986 1106 1166 1226 1286
CTCCTTTCTA AGAAGGACCT ACTTCACTAA TCCTCTTTGGG GACAAAGTGT TTATGAAGCA AAGAGTAATA ATGCAGGATG AATATGATAT TATTCACTTT GGGAATCTCT CACAACACCT	1406 1466

TGGGATTAAG ATGAAGTTAG GAAAGTTCAG CCCATATTTA CCACATGGTC GACACTCTCA CTTATATGTA GACATGATTG AGTTGGCCAC AGGAAGAAGA AAGATGCCAT CCTCTGTGTG 1586 CAGTGCAGAT TGTAGTCCTG GATTCAGAAG ATTGTGGAAG GAGGGAATGG CAGCCTGCTG TTTTGTTTGC AGCCCCTGCC CAGAAAATGA AATTTCTAAT GAGACAAGCT CCTCTCCATT 1706 TCATCCTTGC ATTCAGACAG GAACAATTAT GGGCTGGAGA TGTGACTATG GGATGGGAAT 1766 CCCATCACTC ACTTGATGTC CTGTCTTCCG GCTGGAGGTG GGCTCTTTAA GTTAACACTA TCTACTGTAG TACATTTCAT CTAAGGTCTC TGACCTCCCA AGTCTCTGGT GCATTTTGGT GGGTCCACCC ACCCTCCTAT TACCTGAAGT TGCCTGTTTA TATTCTTTTT GCTGGTCCTC AGAGATCGGT TCCCCTCTCA CCTGCCCACA CACCACAAAC CCCTTTCAAA TAACATCATA AATGATACAA TGAAGTTAAG TATACAAAGA ACAAATTGCT TGGTTTTATT TCATTTAAAT CTTTATGAAC TTTATGAATT GAAATCAATG CTCGGCAACA GCATCCTTCA CATTACATAT 2126 CAGCATCAAA GGCAGCATTG CAAGGCTTCT TTCATTACCC TTACTTGAAT TACCTTGACA ATAAAATTTC TGAAGCAGAC CTAACTAAGC TTTCCTTTGG AAATCAGATA TGGATCAATG 2246 TGTGAATTGT CCAGAATACC AATATGCCAA CACAGAACAG AACAAATGTA TTCAGAAAGG 2306 TGTCACCTTC CTAAGCTATG AAGACCCCTT GGGGATGGCA CTTGCCTTAA TGGCCTTCTG 2366 CTTCTCTGCA TTCACAGCTG TGGTACTTTG TGTCTTTGTG AAGCACCATG ACACTCCTAT 2426 TGTGAAGGCC AATAACAGAA GCCTCAGCTA CCTATTACTC ATGTCACTCA TGTTCTGTTT 2486 TCTGTGCTCC TTTTTCTTCA TTGGCCTTCC AAACAGAGCC ATCTGTGTCT TACAGCAAAT 2546 CACATTTGGA ATTGTATTCA CTGTGGCTGT TTCCACAGTT CTGGCCAAAA CAGTCACTGT GGTTCTGGCT TTCAAAGTCA CAGACCCAGG GAGAAGATTG AGAAACTTCC TGGTATCAGG 2666 GACACCCAAC TACATTATTC CCATATGTTC CCTACTCCAA TGTGTTCTGT GTGCAATCTG GCTAGCAGTT TCTCCTCCCT TTGTTGATAT TGATGAACAC ACTCTCCATG GCCATATCAT CATTGTGTGC AACAAGGGCT CAGATACTGC ATTCTACTGT ATCCTGGGAT ATTTGGCCTG 2786 CCTGGCACTT GGAAGCTTCT CTCTGGCCTAG AATCTGCCTG ACACATTCAA 2906 TGAAGCCAAA TTCTTGACCT TCAGCATGCT AGTGTTCTGT AGTGTCTGGG TCACCTTCCT CCCTGTCTAC CATAGCACCA AGGGCAAACA CATGGTTGCT GTGGAGATCT TCTCCATCTT 3026 GGCATCCAGT GCAGGGATCC TTGGATGTAT TTTTGTACCC AAGATTTATA TCATTTTAAT GCGACCAGAG AGAAATTCTA CCCAAAAGAT CAGGGAAAAA TCATATTTCT GAACAAATAT 3146 TTAGGAATTC TGTCAAATGT AAAGTTGGTA CATACCCACC AAATATTGGG TTATAGTGCA 3206 TGTGTCTAGT TTTAGAATCA CTCTCACTGG TTGCTCTAGT GATATCAGGA AGTATCATAT 3266 CTACTGAACT TCCCTACAGT GTCCATAAAA TCTTGCACTC ATTCACTTTC TTCATTTTCT 3326 CTCAGAGAAC TAAACTCTCA ATTATTACAA TTTTATTCTT CATTTTGATT TCATGGAGAT 3386 GGCCCTCTGG TAACTGCCAA AAAATGTTGA TAAGGCAGTT GAATCCACCA CTTTGTGTAG AAAAATGAGA TCTAGGAAGA CAGGGTTACA CATAAAAACC ATCTACCAAA TCAAATAATC AATGAGAAAC ACAGACTAAC TAAATAATCA GCAAAGATGA AATCAGAACA TATTTTCTGA 3566 TTTCCAGTAA GAGCACACA ATAAGAAAAT ACTTACTTTT TTCATCTGTT CTTCAATCTA CTGGCCAATA GTCTAAGGAG GAAATGTTCC TTTTCTGCTG TCAAATAAAA ATATATTATA 3686 TCC

(2) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 127 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Phe Ile Phe Met Gly Val Phe Phe Leu Leu Asn Ile Thr Leu Leu 10 Met Ala Asn Phe Ile Asn Pro Arg Cys Phe Trp Arg Ile Asn Leu Asp 20 25 Glu Ile Thr Asp Glu Tyr Leu Gly Leu Ser Cys Thr Phe Ile Leu Ala **35** . 40 45 Ala Val Gln Thr Pro Thr Glu Lys Asp Tyr Phe Asn Lys Thr Leu Asn 55 60 Val Leu Lys Thr Thr Lys Asn His Lys Tyr Ala Leu Ala Leu Val Phe 70 Ala Met Asp Glu Ile Asn Arg Asn Pro Asp Leu Leu Pro Asn Met Ser Leu Ile Ile Arg Tyr Thr Leu Gly Leu Cys Asp Gly Lys Thr Val Thr . Pro Thr Pro Tyr Leu Phe His Lys Lys Lys Thr Lys Pro Tyr Pro 115 120 125

- (2) INFORMATION FOR SEQ ID NO:31:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3896 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 36...263
 - (D) OTHER INFORMATION:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

ATTTCACAAC TTCTTGATCT TAGACCTTAG CAGAT ATG AAA AAC CTG TGT GTT Met Lys Asn Leu Cys Val 1 5
TTC ACT CTT TCC TTT TTC CTC CTG GAG TTT TCT CTG ATC TTG TGC CAT Phe Thr Leu Ser Phe Phe Leu Leu Glu Phe Ser Leu Ile Leu Cys His 10 15 20
TTG ACT GAA CCC ATT TGC TTT TGG AGG ATA AAT AAT AAT GAA GAT AAT Leu Thr Glu Pro Ile Cys Phe Trp Arg Ile Asn Asn Asn Glu Asp Asn 25 30 35
GAT GGA GAT TTG AGA AGT GAC TGT GGT TTT TTC CTT GCA GCA GTT GAG Asp Gly Asp Leu Arg Ser Asp Cys Gly Phe Phe Leu Ala Ala Val Glu 40 45 50
GGA CCT ACT GAC GAC TCT TAT AAT ATC TCT GAT CTT AGG TTT TCT TTG Gly Pro Thr Asp Asp Ser Tyr Asn Ile Ser Asp Leu Arg Phe Ser Leu 55 60 65 70
GAC CAT TTA ATC CTA AGC TGAGTGACCA TGACCAGTTT CCCTATGTCC ATCAGGTA 301 Asp His Leu Ile Leu Ser 75
GCCACCAAGG ACACACGTTT GTCCCATGCA ATGGTCTCCT TGATGTTTCA TTTTACATGG 36
ATTTGGATAG GAATGGTCAT CTCAGATGAT GACCAGAGTA TTCAGTTTCT ATCAGACATG 42
AGAGAAGAAA TGCAAAGACA TGGAATCTGT TTAGCTTTTG TTAATATGAT CCCAGAAGAC 48

61 21 81 ATGCAGTTAT ATATGACAAG GGCTACAATA TATGATAAAC AAATTATGGA ATCAACAGCA 541 AAGGTTGTTA TGATTTATGG TGAAATGAAC TCTACCTTAG AAGTTAGCTT TAGAAGGTGG GAAGATTTAA GTATAAGGAG AATCTGGATC ACAACCTCAC AATGGGACGT TATCACAAAT 601 661 AAAAATGATT TCAGCCTTGA TTTCTTCCAA GGGACTGTCA CTTTTGCACA CCATGTAGGT 721 GAAATTGCTA ACTTTAGGAA TTTCTTGCAA ACAATGAACA GTGAAAAATA CACAGTAAAC 781 ATTTCTGAGT CTAGACTGGG GTGGAATTAT TTTAATTGTT CCATCTCTAA GAACAGCAAT 841 AAAAAGGATC ATTTTACATT CAACAACACA TTGGAATGGA CAACACTGCA CAAATATGAC ATGGTCCTAA GTGAGGAAGG CTACAATTTG TATAATGCTG TGTATGCTGT GGCCCACACC 901 961 TACCATGAAC TCGTTCTTCA ACAAGTAGAA TCTCAGCAAA TGACAGTACC CAAAGGAACA TTCACTGACT GTCAGCAGGT GTCTTCCATG CTGAAGTCCA GGATATTTAC TAACCCTGTT 1081 GGAGAACTGG TGAACATGAA GCATAGGGAA AATCAGTGTA CAGAGTATGA TATTTTCATC 1141 ATTTGGAATT TTCCACAAGG CCTTGGATTA AAAGTGAAAA TAGGAAGCTA TTTGCCTTGT 1201 TTCCAACAGA GCCAACAACT TCATATATCT GAAGATTTGG AGTGGGCCAC AGGAGGATCA 1261 TCAGTACCCC CCTCCTGTG TAGTGTAACA TGTACTGCTG GATTCAGGAA AATTCATCAG 1321 AAACAAACAG CAGACTGCTG CTTTGATTGT GATCAGTGCC CAGAAAATGC AGTTTCCAAT 1381 GAAACAGAGA TATGCAATCT GAACATGGAA AGACCATCAT TATTTGCAAC AAAGGCTCAG 1441

TAATTGCCTT CCACTTTGTT CTCGGATACT TGGGTGCCTT GGCTCTGGGG AGCTTTACTG TGGCTTTCTT GGCTAGGAAC CTTCCTGACA GATTCAATGA AGCCAAATTC TTAACCTTCA GCATGCTGGT GTTCTGCAGT GTCTGGATCA CCTTCCTCCC TGTCTACCAC AGCACCCAGG GAACGGTCAT GGTGGTTGTG GAGGTTTTCT CCATCTTGGC TTCTAGTGCA GGCTTGCTAG GGTGTATCTT TCTCCCAAAA TGTTGTGTTT TATTACGTAT ACAAAATTCA AACTTTCTGC ATAAGTACAA ACATGAATTG CATTCTTGAT TCTTTAGTAA TTTAAAAATG CTAATCATAC TCAACTTATC TTTTTGCTTT GTCATAACAA AAGCACCACT AAATCATACA AAAAATTTAA GTAATATACA AATTTAGTAT TTACAATGTA GGGCAGCACA GCACTGCCTA ATGTAATGCC AATTATTGTT TTAGAGGTAA ATGGTCTTAT TCATGTGTAC ATAGATGTAA ACATTGAGAA TAGGGAATCT AACTTGATGA ATGGCTATCA ACACTTTGAC CTCTAGGTAT GTGTGTAAGC CATGTACCTA ATTTAATATG TAATAAGGTG AGCGTAACAT ATGTGAGAGT GCTACCTCTG GGCAGAAAGT TCTGGGAATT ATAAGAAAGA GGACTTCAAA GAGCACAGGC ATGAAGTCAA TAATCAGCAT TATTCCATGT GCTCTCATTG AGTGTCTGCA TCCACGTTCT TGTCTTGACT TCATTCTATT AACTGTGACT AAGGTACATA GGGAAATAGG ACTTTTCTCA CATGGTTCCT TTGACCATGG TGTTTTCTTA CAGCAACAGA CTCTAAGACA TCAGCAAAAT GTTAAATTGC CTTGGTTAGG ATTTGGAATA TCACAGATTA CTGATGCAAT AGAAGGCACT GATTTGAAAG AGAAAATAGA TTGAATACTA GGGGAGTGTG AGCATAGTTA CAGTGTTGCA TATTGTTGAT GGCCATCACA GAGGCCTGAG ATTTGTAATT GCTTCATAAT GTACTATGAA AATATTCAGA 2521 ATATCAGGTA ACATACTAAA AGAAGTACAA TATATGAAAA GGACAATGGG GTTCAGATTA TGCCTGCTCT ATAAGGCTCA TGAACTTCAT ATGAAAACAT ACCATTTCAA TATGAAATGA AGAAGTTTCA TTCAGGGAGA AAAATTGGTA GTGGAAAAAT TTACACACAA GACCTATATC ACAAGGAGAT CAGTGAAATC TTGGAATATA TAAGGCACTC TAGAAGAATG ACTTCAAAAA TGTTAGCAAA ATAGGAACAA CTAAGAATTA TTTGGTTTAA TATTACATAA TCAAAGATGT ACATACAAAC ACATGAACAT TATTATTTCT GGACGTCAGT TGCTGAAGGT CAGTGTCATT TTCTCTCAAA GTATTGTTTG TTGCTCTTAT TTTACTTGTT AATTTACAGT TTATTTTTGA 2941 TGGGATAATT TAATTGTTTT TTTCTTTATA TTTCCTGTCT CAAGAACACC ACTTGTAGCC CATCCATACA CTCCTAAAAT GCAAATGACC TATTATTTCA TTAATGCTTA ATGAATGCAT 3061 GCATGTATTT GTATATACAT ATACATTTTA AAGTATACAT TGTAGATACT ATGTAAAATT GCATGTTTTT ATGTTTTGAT GGCTCATTAT TTGGTAATAC CTGGCCAATA TTTGTTCCCT TCCCTGGCTA TGACAACCTC CTCCATTCCC TGATTTAAAG TTTCCTGTAA ATGGTTGTGT AGGGTAGAAG CTTTGAAAGC TTTCTTCCTT CCACGCTGCC ATGCACAGTG CAGTAATCCT TCTTCAGACC ATATTTTGTG TGTCATATTG GTAAAACTTC ATGGTCTACT TATGCTAGTT CTAGAAGATT TGTGTTCACA GCCAGTTTCC TCATCCTTTG ACTCACAAGA TCTTTTCCAC 3421 CATCTTCTTT ACGTTTCTCT GAGCCTTGGA TGAGGGAAAA TTTTGTAAGA GGATACATTG AATTGTTTCC TTCAACTACC TACTCTGGAA ATGACTATCA CACTATCACA ACATCTTTAA AAACAAGATG GAACTCCAAA ATCATTTTCT AAGGAAATAA ATGAAAATCT AAGTGTTCTT TTAATCTGGT TCATTGGAAT TTCCTGCATT TATCTGCCTG GGTGTATGTA ATCCCCCCCC CCCAGCCTGA AACCTGGCTG AACAGGTTTC ACTGTTAGCA CGAAGAGAGA ATCCGGGGTG 3721 GAGCCTTCCA CCCTATCATT CTGCCACTCC CACTGCTACT GCCTGCCGCC CAGCTGTTCC GGAGCTATCA CGTGGTCACC TGAAATTGGA CTCCAAGGAT GATTTGGAGG GAATGGGTGC 3841 CTTCCCCTTC TTCATAAACC AGTGTCTGGG AATAGTAAAA TTGAACTTTG ATCAG

(2) INFORMATION FOR SEQ ID NO:32:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 76 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

 Met
 Lys
 Asn
 Leu
 Cys
 Val
 Phe
 Thr
 Leu
 Ser
 Phe
 Phe
 Leu
 Glu
 Phe
 15
 15

 Ser
 Leu
 Ile
 Leu
 Cys
 His
 Leu
 Thr
 Glu
 Pro
 Ile
 Cys
 Phe
 Trp
 Arg
 Ile

 Asn
 Ile
 Ser
 Tyr
 Asn
 Ile
 Ser

 Asn
 Leu
 Arg
 Phe
 Ser
 Leu
 Asn
 His
 Leu
 Leu
 Ser
 Ile
 Ser
 Ile
 Ser
 Ile
 Ser
 Ile
 Ile
 Ser
 Ile

(2) INFORMATION FOR SEQ ID NO:33:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2811 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
 (ix) FEATURE:
- - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 962...2605
 - (D) OTHER INFORMATION: GOVN1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

ACTICATATE GGACCATTGC AACCCCTTCC TGCTAACTG AATCAGGATA CCTCGTACAC CAGGATGGAG CTGTGGTCAT TGGTGCATT TTTCTGTTT TAAAGTCCTT GCCTATAAGT CAAATAATAG ATTGGAAAAC ATTATCTTTT GACACATACA ATTCTTATAG GATAAAATGCA 240 CAAATATCAC AACTTGTTTT GGCCATGATA TTTGCGATCA ATGAGATCAA TGTGAAATGCA 360 AATATCTCA GAGGTGCACT ACTTGGGCTC GCACTTACTG GCAAATCCAT TCCTAAATAC ACATGCAGAA AGGATACCAA ATCAGCTCT GAGATTTATA ATCTGCCATA TTTTGAACGG 360 AATATCTCA GGAGTGCACA ATCAGCTCT GAGATTTATA ATCTGCCATA TTTTGAACGG ACACCTCTG GGACTTTGTT GGACATTTAC AAATTTCCTC AGCATAAATTC TCCTAAATTAC GAGACCTTTG GGACTTTGT GGACATTTAC AAATTTCCTC AGCTTAACTT TGGGCCGTGT GACACGGAGA AGCACAGTTT CCACTCTTG AAATTCCTC AGCTTAATT TGGGCCGTGT GACACGTGTT CAGATAGCAG AAACCAGTTT CCACTCGTT ACCAGGTGGC CCCCAAAGAC ACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCAT TCAACTGGAC CTGGGGGGGA CACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCAT TCAACTGGAC CTGGGGGGGA CACACCTCTGT TCTGTGGTAT CACCTCTTTG GAAACACAGA AAAGGAACCG CTGCTAAATCA CAGAGGTACA CAGAGGTTCT CAGTTCATT TCAACTGGAC CTGGGGGGGA CACACCTCTGT TCTGTGGTAT CACCACTCTTG GAAACACAGA AAAGGAACCG CTGCTAAATCA CAGAGGTTCT CAGTTCATAT TCAACTGGAC CTGGGGGGGA CACACCTCTG TACCCCAAA TCAGAGGACCT CAGTTCATT TCAACTGGAC ATTTTTTTTGG GGAAATCATTG GACAAGAAAAA AATTTTCTTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGGTAACA CATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG MET Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1
GAAATAATAG ATTGGAAAAC ATTACTTTT GACACATACA ATTCTTATG GATAAATGCA CAAATAGCAC AACTTGTTTT GGCCATGATA TTTGGGATCA ATGAGATCAA TGTGAAGTCC CATAATTACC AACTTGTTTT GGCCATGATA TTTGGACTCA ATGAGATCAA TGTGAAGTCC CATAATTACC CAAATACCTC TCTGGGACTT GAGAGTTCA ATCAGGACTAA TTTTGAACGG AATATTCTGA GGAGTGCACT ATCTTGGCTC ACAGGCTTGA GCAAATTCAT TCCTAAATAC CACTGCAGAA AGGATAGCAA ATCAGCTGCT GCACTTACTG GAATATCACA GAAAAAACATCT GAGACCTTTG GGACATTTAC AAAATTCTCT AGCTTAATTT TGGGCCGTGT 540 GATCCTGTT AGATAGGCAG AAACCAGTTT CCATCTGTGT ACCAGGTGGC CCCCAAAGAC CACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA CACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA CACACTACTG TCTGTGGTAT CACCTCTTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA CACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTTGG GGAATCATTG CATTATATGC TAACCCACAAA TCAGAGTGCTA ACCTTTGTG GAAACAGTAA TATTTTTTTGG GGAATCATTG CATTATATGC TAACCCACAAA TCAGAATGCAAA ACCTTCAGAGT CATCAGCAAA TGTGATTATAA ATTGGATAGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTG AACAATATAC CATG TTA GAA TTGGGC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 25 30 TAC CCA GAA GAC ATT TTT CTC CAC ATC TTG TGG AAC CAG TAT TTC AAT Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 40 45 TGT CCA CTT TTG GAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 60 AAT GCC TCT TTG GAA TTG TCG CA GGG GGT GTT TTT GAG CTG GTC ATG ASn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 70 75 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA CCC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
CARATGTACC AACTTGTTTT GGCCATGATA TTTGCGATCA ATGAGATCAA TGTGAAGTCC 360 CATATATTTAC CANATACCTC TCTGGGACTT GAGGTCTAA ATCTGGCTAA ATCTGGCAAA ATCAGGTGCAA ATCAGGTTGAA GCAGGCTTAATTCAA 420 ACCTGCAGAA AGGATGCAA ATCAGCTGCT GCAGGTTTACG GCACATTACTG GAATATCACA GAAAACATCT 480 GAGCACTTTGT GGACATTTACA AAATTTCCTC AGCATGTGT ACCAGGTGGC CCCCAAAGAC 600 ACACCTCTGT TCTGTGGTAT CACCTCTTTG ACCACTCTATT TCCACTCTGTT TCCACTCTGTT TCAACTGGAC CCCCAAAGAC 600 ACACCTCTGT TCTGTGGTAT CACCTCTTTG ACCACTTAATT TCCACATAATTACAACAAAATACACAAAAAAAAAAAAA
CATATTTTCA CAAATACCTC TCTGGGACTT GAGATTTATA ATCTGCCATA TTTTGAACGG AATATTCTGA GGAGTGCACT ATCTTGCTC ACAGGCTTGA GCAAATTCAT TCCTAATTAC 420 ACCTGCAGAA AGGATAGCAA ATCAGCTGCT GCACTTACTG GAAATTCACA GAAAACACTT 480 GAGACCTTTG GGACTTTGTT GGACATTTAC AAATTTCCTC AGCTTAATTT TGGGCCGTGT 540 GATACCTGTTC AGATAGCAA ATCAGCTGCT CCAACCTGTGT ACCAGGTGGC CCCCAAAGAC 660 ACACCTCTGT TCTGTGGTAT CACCTCTTG AGCTTCTGTT ACCAGGTGGC CCCCAAAGAC 660 ACACCTCTGT TCTGTGGTAT CACCTCTTGT AGCTTCATT TCAACTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTCTAT CAGAGGTTAG AAAGGAGCTG 720 GACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACACTAA TATTTTTTGG GGAATCATTG 780 CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA 840 GTTTATATGC TAACCCACAA TCAGATGACAA ACTCTAAAAA TGAAACACAG AAAGAATAA 900 ATTATATGGAC ATTTGGTTAT TCAATTAATT GTAATACAAA GTAAACACAG AAAGAATAAC 900 Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1009 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CCC CAT CAT GGG GAG ATC CCC CAT CAT GGG ACC CCC AGA GAC ATC TTT CAC ACC ACC CCC ATC ATC AAG COC CCT ACC AGG COC ACC CCC ACC CCC ACC CCC CAC ACC CCC ACC CCC CCC CCC ACC CCC
AATATTCTGA GGAGTGCACT ATCTTGGCTC ACAGGCTTGA GCAAATTCAT TCCTAATTAC ACCTGCAGAA AGGATAGCAA ATCAGCTGCT GCACTTACTG GAATATCACA GAAAACATCT 480 GAGACCTTTG GGACTTTGTT GGACATTTAC AAATTTCCTC AGCTTAATTT TGGGCCGTGT 540 GACACCTCTGT TCTGTGGTAT CACCTCTTG ATGCTTGTA ACCAGGTGGC CCCCAAAGAC 600 ACACCTCTGT TCTGTGGTAT CACCTCTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT CAGAGGTTGC CCCCAAAGAC 600 ACACACATACA CAGATGACAA CAGAGGTTCT CAGTTTCTAT TCAACTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT TCAACTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT CAGAGGTTAAG AAAGAGATGA AAATCTGCAA ACCTCTTGTG GAACACTAA TATTTTTTG GGAATCATTG 780 CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA 840 GTTTATGGAC ATTTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTG AACAATATAC 960 ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTG AACAATATAC 960 Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1009 TAC CCA GAA GAC ATT TTT CTC CAC ATC TTG TGG AAC CAG TAT TTC AAT TYP Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 40 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 TGT CCA CTT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAA CTG ATG 1105 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAA CTG ATG 1201 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAA CTG ATG 1201 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAA CTG GTC ATG 153 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC T1249 TAC GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC T147 TAT Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
ACCTGCAGAA AGGATAGCAA ATCAGCTGCT GCACTTACTG GAATATCACA GAAAACATCT GAGACCTTTG GGACTTTGTT GAGACATTAC AAAATTTCCTC AGGTTAATTT TGGGCCGTGT 540 GATCCTGTTC AGATAGGCAG AAACCAGTTT CCATCTGTGT ACCAGGTGGC CCCCAAAGAC ACACCTCTTT AGACCACCAC ACCCCTTTTG ATGCTTCATT TCAGCTGGAC CCCCCAAAGAC ACACCTCTTTG ATGCTTCATT TCAGCTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTCTATT CAGAGTAGAC AAAGCAGCT 720 GACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATCATTG 780 CATTATATATC TAACCCACAA TCAGATGCAGA ACCTCTAGAGT CATCAGCAAA TGTGGATCATTG CATTATATATC TAACCCACAA TCAGATGCAGA TCAGATGAGA ACCTCAAAA TGTGATTATA 840 GTTTATGGAC ATTTTGGTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA 900 ATGAAAAAAAA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTAC AACAATTATAC 960 Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1009 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1009 15 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT TYP Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 40 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 55 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG 1201 Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 75 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC TLAT GLU Glu Ser Tyr Asn Val Tyr Asn Ala Val Ala His
GAGACCTTTG GGACTTTGTT GGACATTTAC AAATTTCCTC AGCTTAATTT TGGGCCGTGT GATACCTGTTC AGATAGGCAG AAACCAGTTT CCATCTGTGT ACCAGGTGGC CCCCAAAGAC 600 ACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA 660 CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT CAGAGTTAAG AAAGGAGCTG 720 GACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATTATA 840 CTTTATGGAC ATTTTGCTTT TCAATTAATT GTAAATACAAA GTAAACACAA TAGGATTATA 840 CTTTATGGAC ATTTTGGTTT TCAATTAATT GTAAATACAAA GTAAACACAG AAAGTATTAA 900 ATGAAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAATTG AACAATATAC 960 Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 960 1009 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 960 1009 15 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1057 15 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 15 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 150 150 150 150 150 150 150 150 150 150
GATCCTGTTC AGATAGGCAG AAACCAGTTT CCATCTGTGT ACCAGGTGGC CCCCAAAGAC ACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCTATT TCAACTGGAC CTGGTGGGA ACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCTATT TCAACTGGAC CTGGGTGGGA CTGCTAATCA CAGAGTACAA CAGAGGTTCT CAGTTTCTAT TCAACTGGAC CTGGGTGGGA CACAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATCATTG CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA GTATATAGCA ATTTTGGTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATACA ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTG AACAATATAC C ATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TCC CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1
ACACCTCTGT TCTGTGGTAT CACCTCTTTG ATGCTTCATT TCAACTGGAC CTGGGTGGGA CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT CAGAGTTAAG AAAGAAGCTG 720 6ACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATCATTG 780 CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA 840 GTTTATGGAC ATTTTGCTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA 900 ATGAAAAAGA TTTTGGGTCAT AACCTCAAAA TGGGTTGGC AAAAAAATTG AACAATATAC 960 CATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG MET Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 10 15 15 10 15 15 10 15 15 10 10 15 15 15 10 10 15 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 15 15 10 10 10 15 15 10 10 10 10 10 10 10 10 10 10 10 10 10
CTGCTAATCA CAGATGACAA CAGAGGTTCT CAGTTTCTAT CAGAGTTAAG AAAGGAGCTG GACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATCATTG CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA GTTTATATGGAC ATTTTGCTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAATTG AACAATATAC C ATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1
GACAAGAATA AAATCTGCAT AGCCTTTGTG GAAACAGTAA TATTTTTTGG GGAATCATTG CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA GTTTATGGAC ATTTTGCTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATATC CATG GAC ACT CTG ACT TTC TCA CCC CAT CAT GAG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 25 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 40 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 55 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 75 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
CATTATATGC TAACCCACAA TCAGATGCAG ACTCTAGAGT CATCAGCAAA TGTGATTATA GTTTATGGAC ATTTTGCTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAATTG AACAATATAC C ATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1
GTTTTATGGAC ATTTTGCTTT TCAATTAATT GTAATACAAA GTAAACACAG AAAGTATGAA ATGAAAAAGA TTTGGGTCAT AACCTCAAAA TGGGTTGGCC AAAAAAAATTG AACAATATAC C ATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 25 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT TYR Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 40 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 55 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 75 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
ATGARARAGA TTTGGGTCAT ARCCTCARAR TGGGTTGGCC ARARARATTG ARCARTATAC C ATG TTA GAR TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1 5 10 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 25 30 1057 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 40 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 55 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 75 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
C ATG TTA GAA TTG GCC CAT GGC ACT CTG ACT TTC TCA CCC CAT CAT GGG Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 15 GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT TTY Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 35 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG 1201 Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 1
GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1057 Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1105 Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG 1201 Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
GAG ATT TCT GAT TTC ACA AAT TTT ATG CAG GAA GTC ACC CCT ATC AAG 1057 Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1105 Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG ATG ASn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1105 Tyr Pro Glu Asp Ile Phe Leu His And ATC TTT GAA AAC CAG TAT TYr Phe Asn TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Pro Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 30 TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1105 Tyr Pro Glu Asp Ile Phe Leu His And ATC TTT GAA AAC CAG TAT TYr Phe Asn TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Pro Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT 1105 TYr Pro Glu Asp Ile Phe Leu His at 1 le Leu Trp Asn Gln Tyr Phe Asn Gln Tyr Phe Asn TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 60 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG ANG ASN AND Cys Ile Pro 65 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
TAC CCA GAA GAC ATT TTT CTT CAC ATC TTG TGG AAC CAG TAT TTC AAT TTC TYP Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG ASn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 70 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG ASn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Tyr Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn 45 TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG ASn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC 1249 Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
TGT CCA CTT TTG CAT TCT GAG TGT AAA ATC TTT GAA AAC TGT ATA CCC 1153 Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 70 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 70 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro 50 AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 70 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
AAT GCC TCT TTG GAA TTG TTG CCA GGG GGT GTT TTT GAG CTG GTC ATG Asn Ala Ser Leu Glu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met 65 70 80 ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
ACT GAA GAG AGT TAC AAT GTG TAC AAT GCT GTG TAT GCA GTG GCC CAC Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His
2.
AGT CTC CAT GAG AAG GCT CTC CAT CAA GTA GAA ATT CAA CCA CAG GAT 1297
Ser Leu His Glu Lys Ala Leu His Gln Val Glu Ile Gln Pro Gln Asp
100 105 110
200
AAT AAA GAT AGG ACT ATA TTA TTT CCT TGG CAG CTT CAC CCT TTT CTG 1345
Asn Lys Asp Arg Thr Ile Leu Phe Pro Trp Gln Leu His Pro Phe Leu
115 120 125

			CAG Gln													1393
			AAG Lys													1441
			GGT Gly				•									1489
			AAG Lys 180													1537
			GGA Gly													1585
			GGA Gly													1633
			TGC Cys													1681
			CAG Gln													1729
			CAC His 260													1777
			GGG Gly													1825
			CTT Leu													1873
			GCC Ala													1921
			TGT Cys													1969
			TGT Cys 340													2017
			TCC Ser													2065
			ACT Thr												TTA Leu	2113
AGA	GCC	CCT	CAG	TTC	ATC	ATT	CCA	CTT	TGT	GCC	CTG	ATG	CAA	ATC	CTT .	2161

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Arg 385	Ala	Pro	Gln	Phe	Ile 390	Ile	Pro	Leu	Cys	Ala 395	Leu	Met	Gln	Ile	Leu 400	
		GGG Gly														2209
		TCT Ser														2257
		GGC Gly 435														2305
		TAC Tyr														2353
		TCC Ser														2401
		ACA Thr														2449
		ATG Met														2497
		ATC Ile 515						Tyr								2545
		ATA Ile														2593
		GAA Glu		TAG	CAGTO	CAA (JACA!	\ACA1	TT GO	ECT1	AGCA	LAA	AATG:	rctg	ATTGT	2650
GAC	AGAC		'GAT	ATTG	T TO	CAAA:	CTATO	TAJ	LAAT	\TGT	GAC				ACATGA BACCAA	2710 2770

(2) INFORMATION FOR SEQ ID NO:34:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 548 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Met Leu Glu Leu Ala His Gly Thr Leu Thr Phe Ser Pro His His Gly 10 Glu Ile Ser Asp Phe Thr Asn Phe Met Gln Glu Val Thr Pro Ile Lys 20 25 Tyr. Pro Glu Asp Ile Phe Leu His Ile Leu Trp Asn Gln Tyr Phe Asn .

Cys Pro Leu Leu His Ser Glu Cys Lys Ile Phe Glu Asn Cys Ile Pro Asn Ala Ser Leu Glu Leu Leu Pro Gly Gly Val Phe Glu Leu Val Met Thr Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His Ser Leu His Glu Lys Ala Leu His Gln Val Glu Ile Gln Pro Gln Asp Asn Lys Asp Arg Thr Ile Leu Phe Pro Trp Gln Leu His Pro Phe Leu Lys Asn Ile Gln Leu Ile Asn Ser Val Gly Asp Arg Val Ile Leu Asp Trp Lys Lys Lys Thr Asp Thr Glu Tyr Asp Ile Ser Asn Ile Trp Asn Phe Pro Thr Gly Leu Ser Leu Leu Val Lys Val Gly Thr Phe Ala Pro Ser Ala Pro Lys Gly Glu Gln Leu Ser Ile Ser Glu His Thr Ile Asn Trp Pro Ile Gly Phe Thr Glu Ile Pro Lys Ser Val Cys Ser Glu Ser Cys Ser Pro Gly His Arg Lys Val Ile Leu Glu Ser Lys Pro Ala Cys Cys Phe Asp Cys Thr Pro Cys Pro Asp Lys Glu Ile Ser Asn Glu Thr Asp Val Gly Gln Cys Val Lys Cys Pro Glu Ser His Tyr Ala Asn Thr Glu Lys Ser His Cys Leu Lys Lys Thr Met Thr Phe Leu Asp Tyr Asn Asp Ser Leu Gly Thr Gly Leu Thr Leu Met Ser Leu Gly Phe Phe Val Val Thr Gly Leu Val Ile Gly Val Phe Ile Ile His Arg Asn Thr Pro Ile Val Lys Ala Asn Asn Arg Ser Leu Ser Tyr Ile Leu Leu Ile Thr Leu Thr Leu Cys Phe Leu Cys Pro Leu Leu Phe Ile Gly Leu Pro Asn Thr Ala Thr Cys Ile Leu Gln Gln Asn Leu Phe Gly Leu Leu Phe Thr Val Ala Leu Ser Thr Val Leu Ala Lys Thr Ile Thr Val Val Met Ala Phe Lys Ile Thr Ala Pro Gly Arg Lys Thr Arg Trp Leu Leu Ile Leu Arg Ala Pro Gln Phe Ile Ile Pro Leu Cys Ala Leu Met Gln Ile Leu Phe Ser Gly Ile Trp Leu Gly Thr Ser Pro Pro Phe Val Asp Met Asp Ala His Ser Glu His Gly His Ile Ile Leu Cys Asn Lys Gly Ser Ala Ile Gly Phe Tyr Cys Thr Leu Ala Tyr Leu Gly Val Met Ala Phe Gly Ser Tyr Leu Leu Ala Phe Met Ser Arg Asn Leu Pro Asp Thr Phe Asn Glu Ser Lys Ala Leu Ala Phe Ser Met Leu Met Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr His Ser Thr Thr Gly Lys Val Arg Val Ala Met Glu Met Phe Ser Ile Leu Ala Ser Ser Ala Ser Ile Leu Thr Leu Ile Phe Val Pro Lys Cys Tyr Ile Val Leu Phe Arg Pro Glu Arg Asn Ile Leu Pro Leu Asn Arg Glu Lys Arg Gln His Arg Ser Lys Asn Ser Glu Thr

(2) INFORMATION FOR SEQ ID NO:35:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 3584 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA (ix) FEATURE:

(A) NAME/KEY: Coding Sequence(B) LOCATION: 273...2576(D) OTHER INFORMATION: GOVN2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

	_	-							-							
															TCCTT	60
CTCC	CACCA	ATC (CACTI	CTC	AT GO	CAA	TTTC	: ATC	GATO	CCT	GGT	CTTI	TG (BAGA	CAAAT	120
TTG	ATG	AG 1	CAAC	GAAZ	VA AA	ACT1	'GGA'	TA T	LAATI	GTG	CCTI	CATO	CT 7	CGGAC	CAGTT	180
CAGT	TGC	TA 1	rggae	DAAA	A T	TTTC	CAATO	AGA	CTTI	GAA	TGTC	CTAP	AA A	CAAC	TAAAA	240
ACAZ	CAA	ATA 7	rgcc1	TGG	CA TI	AGC	TTT	CA	ATG	GAG	GAA	ATC	AAC	AGG	AAC	293
									Met	Glu	Glu	Ile	Asn	Ara	Asn	
									1				5			
			TTA													341
Pro	Asp	Leu	Leu	Pro	Asn	Met		Leu	Val	Ile	Lys	His	Thr	Leu	Ser	
		10					15					20				
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			Gly													303
IAT	25	Asp	Gry	ABII	1111	30	Asp	urs	116	FIIE	цув 35	GIU	гур	PILE	IYI	
	23					30					35					
AAG	CCT	TTA	CCT	AAT	TAT	GTC	TGT	AAT	GAA	GAG	ACT	ATG	TGT	TCA	TTT	437
			Pro													
40					45		-1-			50			-1-		55	
															-	
ATG	CTT	ATA	GGG	CTG	AAT	TGG	GTA	TTG	TCT	CTA	ACA	CTT	TTT	AAA	GAC	485
Met	Leu	Ile	Gly	Leu	Asn	Trp	Val	Leu	Ser	Leu	Thr	Leu	Phe	Lys	Asp	
			•	60		-			65					70	-	
TTG	GAC	ATC	TTC	TCA	TTT	CCA	CGT	TTC	CTT	CAA	ATT	TCC	TAT	GGA	CCT	533
Leu	Asp	Ile	Phe	Ser	Phe	Pro	Arg	Phe	Leu	Gln	Ile	Ser	Tyr	Gly	Pro	
			75					80					85			
			ATC													581
Phe	His	Ser	Ile	Phe	Ser	Asp	Asn	Glu	Gln	Phe	Pro	Tyr	Leu	Tyr	Gln	
		90					95					100			•	
3.000		~~~		~~~		mar	~~~	~~~	mma	663	3 000	ama		mma		620
			AAG													629
Met		Pro	Lys	Asp	Thr		Leu	Ala	Leu	Ala		var	ser	Pne	ren	
	105					110					115					
COUNT	тас	שיזירי	AAT	TCC	ממ	TCC	CITT	GGG	حبي	CTC	አጥር	ጥርጥ	CAT	ייממ	CAT	677
			Asn													0,,
120	TYL	FIIG	ASII	TTD	125	ırp	val	Gry	neu	130	116	Ser	ASD	ASII	135	
120					125					130					133	
GAA	GGC	AAT	CAA	TTT	CTC	TCA	GAG	TTG	AAA	AAA	GAG	ACC	CAA	AAC	AAG	725
			Gln													
	1			140					145	-1-			~ ••	150	-, -	
GAA	ATT	TGC	TTT	GCC	TTT	GTT	AAC	ATG	ATG	TCA	ATC	CAT	GAG	CAT	TCA	773
			Phe													
		- , _	155					160					165			
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mcm.	m » m	CAA		» Cm	GB 8	» mo	ma c	m» c	220	GD 3	3 m 3	ama.	» ma	man		
													Met		TCA Ser	821
													ATT Ile		TTG Leu	869
													TGG Trp		ACA Thr 215	917
													ACT Thr			965
													GAG Glu 245			1013
GGA Gly	TTT Phe	ACA Thr 250	AAT Asn	TTT Phe	TTC Phe	GAG Glu	ACA Thr 255	TGG Trp	GAC Asp	CAT His	CTC Leu	AGA Arg 260	AGC Ser	AGA Arg	GAT Asp	1061
TTA Leu	AAT Asn 265	CTA Leu	TTA Leu	ATA Ile	CCA Pro	GAG Glu 270	TGG Trp	AAG Lys	TAC Tyr	TTT Phe	AGC Ser 275	TAT Tyr	GAT Asp	GCC Ala	TCA Ser	1109
													GCC Ala			1157
													GAT Asp			1205
													CTC Leu 325			1253
													GGG Gly			1301
													AAG Lys			1349
													AGA Arg			1397
													TCA Ser			1445
													TTT Phe 405			1493
													GCC Ala			1541
AGT	AGA	AAG	ATG	CCG	TCC	TCT	GTG	TGC	AGT	GCA	GAT	TGT	AGT	CCT	GGA .	1589

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Ser	Arg 425	Lys	Met	Pro	Ser	Ser 430	Val	Cys	Ser	Ala	Asp 435	Cys	Ser	Pro	Gly	
			TCC Ser													1637
			CCT Pro													1685
			TGT Cys 475												AAA Lys	1733
			AAA Lys													1781
			GCC Ala													1829
			GTC Val													1877
			ATC Ile													1925
TTT Phe	CTC Leu	TGC Cys	TCC Ser 555	TTT Phe	TTC Phe	TTC Phe	ATT Ile	GGC Gly 560	CAT His	CCT Pro	AAC Asn	AGA Arg	GGT Gly 565	ACC Thr	TGT Cys	1973
			CAA Gln													2021
			GCC Ala												AGA Arg	2069
		_	AGA Arg													2117
			CCT Pro	-												2165
			GTT Val 635													2213
	Gly		ATC Ile													2261
			CTA Leu													2309
			TTG Leu												AAG Lys .	2357

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680 68	85 6	90	695
TTC TTG ACC TTC AGC AT Phe Leu Thr Phe Ser Me 700			
CTC CCT GTG TAC CAT AC Leu Pro Val Tyr His Se 715			
ATC TTC TCT ATC TTG GO Ile Phe Ser Ile Leu Al 730			
GCA CCC AAA ATC TAC AT Ala Pro Lys Ile Tyr II 745			
CAA AAG TTC AGG GAG AA Gln Lys Phe Arg Glu Ly 760 76		AAATA TTTCAGGAAT T	TAGTTG 2603
AATATTAAGT TGGTATATAC	CCACCAAATA TTTGGTTA	TT GTGCATGTAT AGAG	TTTTAG 2663
AATCAGTCTT ACTGATTCCT	CTATTGCTGT CTAGAGGT	AT CTTATCTACC AGTC	TTGCAT 2723
ACATTGTCCA TAAAATCTTG	TACTCATTCA CTTCTTTA	GT TTCCTCTGAG AAAA	CTAAAT 2783
TTCTCAAATT ATTACTAAAA	TGTAATTCAA CATTATGO	TT TCATGGATAT TTCC	CCCTGG 2843
TTACATCAGA TAAATTTGAT	AAGACAGCTG ATTTTGTT	CAC CTTATATAGA AGGT.	ATATGA 2903
ATGTCCTGCC TTACAGGACA	GAGAGGAATT ACACTTAG	SAA ACCGTCTATC AAGT	
TTCAATCATA CTGAAAAATA			
CTGTTTTCTA GTCGGAGCAT			
AAGGTTTTGG TCAATAGTCT			
TATTATAGCC AACAATTGAA			
GAGGATCCTG AGAAGGAGGG		+	
ACAAAGAATT TTCAGACACT CCCCAACATA TATGCAACAT			
AACCCCCAAG AGACATGATG			
ACTACTTCTT GATGCTGGGA			
GAAAGGGATA ATGAGTTCAC			
AAAAAAAA AAAAAAAT			3584

(2) INFORMATION FOR SEQ ID NO:36:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 768 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met Glu Glu Ile Asn Arg Asn Pro Asp Leu Leu Pro Asn Met Ser Leu 10 Val Ile Lys His Thr Leu Ser Tyr Cys Asp Gly Asn Thr Ala Asp His 25 20 Ile Phe Lys Glu Lys Phe Tyr Lys Pro Leu Pro Asn Tyr Val Cys Asn 40 45 . 35 Glu Glu Thr Met Cys Ser Phe Met Leu Ile Gly Leu Asn Trp Val Leu 50 55 60 Ser Leu Thr Leu Phe Lys Asp Leu Asp Ile Phe Ser Phe Pro Arg Phe 70 75 Leu Gln Ile Ser Tyr Gly Pro Phe His Ser Ile Phe Ser Asp Asn Glu 85 90

Gln Phe Pro Tyr Leu Tyr Gln Met Thr Pro Lys Asp Thr Ser Leu Ala Leu Ala Ile Val Ser Phe Leu Leu Tyr Phe Asn Trp Asn Trp Val Gly Leu Val Ile Ser Asp Asn Asp Glu Gly Asn Gln Phe Leu Ser Glu Leu Lys Lys Glu Thr Gln Asn Lys Glu Ile Cys Phe Ala Phe Val Asn Met Met Ser Ile His Glu His Ser Ser Tyr Gln Lys Thr Glu Met Tyr Tyr Asn Gln Ile Val Met Ser Ser Thr Asn Ile Ile Ile Tyr Gly Lys Thr Asn Ser Ile Ile Glu Leu Ser Phe Arg Met Trp Val Ser Pro Val Ile Gln Arg Ile Trp Val Thr Asn Ser Glu Leu Asp Phe Pro Thr Ser Met Arg Asp Phe Thr His Gly Thr Phe Tyr Gly Thr Leu Thr Phe Leu His His His Gly Glu Ile Ser Gly Phe Thr Asn Phe Phe Glu Thr Trp Asp His Leu Arg Ser Arg Asp Leu Asn Leu Leu Ile Pro Glu Trp Lys Tyr Phe Ser Tyr Asp Ala Ser Gly Ser Asn Cys Lys Ile Leu Arg Asn Tyr Ser Ser Asn Ala Ser Leu Glu Trp Ile Thr Glu Gln Lys Phe His Met Ala Phe Asn Asp Tyr Ser His Ser Ile Tyr Asn Ala Val Tyr Ala Met Ala His Ala Leu His Glu Thr Asn Leu Gln Glu Val Asp Asn Lys Glu Ile Arg Asn Gly Lys Gly Ala Ser Thr His Cys Leu Lys Val Asn Ser Phe Leu Arg Lys Thr His Phe Thr Asn Ser His Gly Glu Arg Val Ile Met Lys Gln Arg Val Arg Val Gln Glu Asp Tyr Asp Ile Val His Ile Gln Asn Phe Ser Gln His Leu Arg Ile Lys Met Lys Ile Gly Lys Phe Ser Pro Tyr Phe Thr His Gly Gly Pro Phe His Leu Tyr Glu Asp Met Ile Gln Leu Ala Thr Gly Ser Arg Lys Met Pro Ser Ser Val Cys Ser Ala Asp Cys Ser Pro Gly Phe Arg Lys Ser Trp Lys Glu Gly Met Ala Pro Cys Cys Phe Ile Cys Ser Leu Cys Pro Glu Asn Glu Ile Ser Asn Glu Thr Asn Met Asp Gln Cys Val Asn Cys Pro Glu Tyr Gln Tyr Ala Asn Thr Glu Lys Asn Lys Cys Ile Gln Lys Asp Val Ile Phe Leu Ser Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Leu Ile Ala Phe Cys Leu Ser Ala Phe Thr Ala Val Val Leu Trp Val Phe Val Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ile Leu Ser Tyr Ile Leu Ile Met Ser Leu Met Phe Cys Phe Leu Cys Ser Phe Phe Phe Ile Gly His Pro Asn Arg Gly Thr Cys Ile Leu Gln Gln Ile Thr Phe Gly Ile Val Phe Thr Val Ala Val Ser Thr Val Leu Ala Lys Thr Ile Thr Val Ile Leu Ala Phe Lys Leu Arg Asp Pro Gly Arg Ser Leu Arg Asn Phe Leu Val Ser Gly Ala Pro Asn Tyr Ile Ile Pro Ile Cys Ser Leu Leu .

	610					615					620				
Gln 625	Сув	Ile	Leu	Cys	Ala 630	Ile	Trp	Leu	Ala	Val 635	Ser	Pro	Pro	Phe	Val 640
qeA	Ile	Aap	Glu	His 645	Ser	Glu	His	Gly	His 650	Ile	Met	Ile	Val	Cys 655	Asn
Lys	Gly	Ser	Ile 660	Met	Ala	Phe	Tyr	Суз 665	Val	Leu	Gly	Tyr	Leu 670	Ala	Cys
Leu	Ala	Leu 675	Gly	Ser	Phe	Thr	Thr 680	Ala	Phe	Leu	Ala	Lys 685	Asn	Leu	Pro
Asp	Thr 690	Phe	Asn	Glu	Ala	Lys 695	Phe	Leu	Thr	Phe	Ser 700	Met	Leu	Val	Phe
Cys 705	Ser	Val	Trp	Val	Thr 710	Phe	Leu	Pro	Val	Tyr 715	His	Ser	Thr	Arg	Gly 720
Arg	Val	Met	Val	Ala 725	Val	Glu	Ile	Phe	Ser 730	Ile	Leu	Ala	Ser	Ser 735	Ala
Gly	Met	Phe	Gly 740	Cys	Ile	Phe	Ala	Pro 745	Lys	Ile	Tyr	Ile	Ile 750	Leu	Met
Lys	Pro	Glu 755	Arg	Àsn	Ser	Ile	Gln 760	Lys	Phe	Arg	Glu	Lys 765	Ser	Tyr	Phe

(2) INFORMATION FOR SEQ ID NO:37:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3578 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA (ix) FEATURE:
- - (A) NAME/KEY: Coding Sequence (B) LOCATION: 1181...3181 (D) OTHER INFORMATION: GOVN3
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

CTATCTTGAA	GAGTGCTTTT	CTGTGTAACT	TGCTTTGCTG	CACGTTTACA	AATTATTTTT	60
TCTTGGTGAA	ATTACTAAGA	TGTTCTCTTT	TCTGTTTGCA	ATTCTTGTCC	TGAAGCTTTC	120
TTTTCCTTTG	TGCAGTCCAA	TTGACAACCG	TTGTTTTTGG	AGATTAAAAA	CCAAGACATT	180
TTGGGAAGGA	GACAAAGAAC	TTGATTGCTT	TTTTTTTATT	TATACAAGGT	TTGGTCATGT	240
AAAGAATGAA	CAGTTCAGTG	GGAATCTAGA	CAAGCGGTTG	ACATCTAAGA	CTATCCACTT	300
GATTTTGACT	CTTTATTTTG	CCCTTGAAGA	AATAAACAGG	AACCCCCATA	TTCTACCTAA	360
CATTTCACTG	CTAGTTAAAA	TTGAATGTGG	GCTGCTAGAT	GATTGGACAA	TAAACAGTTT	420
ATCTTCTAAA	AGAGAAAAAT	ATCTTCCTAA	CTACTACTGT	ATAAATCAGA	GAAGATATTT	480
AATTGTACTT	ACAGGACCAA	TGTGGTTAGC	ATCTGTCATA	GTTGGGCCAC	TCCTATACAT	540
AACTAAGAGG	CCAGAGATGG	ATCAACTCAA	CTCTTCTGGC	TCAAATTCTT	CCCTAAAGTC	600
ACTAATTGGA	TATGGCTTTA	CTCAGCTTCT	CATTGATTTG	CTTTGCTTGA	ACAATCACTG	660
CCCATTTGTT	TTAGTCTTCT	GTCTCCTTTA	TATTCTGGCT	ACAACTGCCT	CTACTGATGC	720
ACATTGAACT	GCATGAACTC	ACAAATTAAC	TCAACACCAT	TGCACTGCAT	TCTTTGCACT	780
GAGTCTCAAA	AGTCTGGTTT	AACTCTTCTG	CATTGAACTC	AACTGACTAA	TTAGAACTCA	840
GAAATCTGCA	TCCCTCTGTC	TCCTGAGTAC	TTTGATTAAA	GGTGTGTACT	ATCACACCTG	900
CACCTAAACT	TTTCTATACT	AAAAATTTGC	TTTATACTAG	GCTGACCTTG	AACTAAGTGA	960
TCTGCTTGCC	TCTGTCTCCT	GCCTTCCAAG	GAATGCCTAT	TTCCCAGCAG	GATATTTTTT	1020
GCCTACAAGT	CTTCAGATGT	GATCCATTAA	GTATAGTCAT	GTTGCTGGAT	TAAAATTCCT	1080
CTACAGATTT	AATTTTCTGA	TCCTGAGGCT	AGTGAAACTT	TACTATGGGC	CATTTCACCC	1140
TCTCTTGAGC	AACCAAGAAC	TGTATCCATA	TCTTTACCAA	ATG GCT CO	CT AAG GAC	1195
				Met Ala Pi	co Lys Asp	
				1 .	5	

ACA TCT CTG GCA CTG GCC ATG GTT TCT TTG TTT GTC CAT TTC AGC TGG Thr Ser Leu Ala Leu Ala Met Val Ser Leu Phe Val His Phe Ser Trp 15

					GTT Val											1291
					AGA Arg											1339
					GTT Val											1387
					CAG Gln 75											1435
					GAC Asp											1483
					CAA Gln											1531
ATG Met	ATC Ile	ATA Ile 120	AAT Asn	AAT Asn	GGA Gly	AAA Lys	TTC Phe 125	CTC Leu	CTT Leu	AAT Asn	TCC Ser	TTC Phe 130	TAT Tyr	GGG GGG	ACT Thr	1579
					CAC His											1627
					CCT Pro 155											1675
					TAT Tyr											1723
					TGT Cys											1771
					ATG Met											1819
					GTG Val											1867
CAA Gln 230	GCA Ala	GAT Asp	ACA Thr	TGG Trp	CAA Gln 235	ATA Ile	GAT Asp	GAT Asp	GGA Gly	AAA Lys 240	GAA Glu	CCA Pro	GAA Glu	TTT Phe	GAC Asp 245	1915
TCT Ser	TGG Trp	CAG Gln	ATG Met	CTC Leu 250	TCT Ser	TTC Phe	CTG Leu	AGA Arg	AAT Asn 255	ATC Ile	CAA Gln	TTT Phe	ATA Ile	AAC Asn 260	CCT Pro	1963
					AAC Asn											2011
TAT	GAG	ATT	CAC	CAG	ACT	TTG	ACT	TTT	TTG	CCA	AAT	CCT	GTA	TTT	AAG .	2059

																•
Tyr	Glu	Ile 280	His	Gln	Thr	Leu	Thr 285	Phe	Leu	Pro	Asn	Pro 290	Val	Phe	Lys	
	AAA Lys 295															2107
	ATG Met															2155
CCA Pro	ACC Thr	TCA Ser	GTT Val	TGC Cys 330	AGT Ser	ATT Ile	CCT Pro	TGT Cys	AGT Ser 335	CCA Pro	GGA Gly	TTC Phe	AGA Arg	AAA Lys 340	TCC Ser	2203
CCT	CAG Gln	CTG Leu	GGA Gly 345	AAG Lys	CCT Pro	GTT Val	TGC Cys	TGT Cys 350	TTT Phe	GAT Asp	TGT Cys	ACA Thr	CCC Pro 355	TGC Cys	CCA Pro	2251
GAA Glu	AAT Asn	GAA Glu 360	ATT Ile	TCC Ser	AAC Asn	ATG Met	ACA Thr 365	AAC Asn	ATG Met	AAT Asn	CAA Gln	TGT Cys 370	ATC Ile	AAG Lys	TGT Cys	2299
	AAT Asn 375															2347
	ATT Ile															2395
	TTG Leu															2443
TTT Phe	TTG Leu	AAG Lys	CAC His 425	CAA Gln	GAA Glu	ACA Thr	CCC Pro	ACT Thr 430	GTC Val	AAG Lys	GCC Ala	AAT Asn	AAT Asn 435	AGA Arg	ACT Thr	2491
CTC Leu	AGC Ser	TAT Tyr 440	GTT Val	CTA Leu	CTC Leu	ATC Ile	TCC Ser 445	CTC Leu	ATC Ile	TCT Ser	TGT Cys	TTT Phe 450	CTC Leu	TGC Cys	TCC Ser	2539
TTG Leu	CTC Leu 455	TTC Phe	ATT Ile	GGT Gly	CAT His	CCC Pro 460	AGC Ser	TTT Phe	ACC Thr	ACA Thr	TGT Cys 465	ATC Ile	ATG Met	CAG Gln	CAG Gln	2587
ACC Thr 470	ACA Thr	TTT Phe	GCT Ala	GTT Val	GTG Val 475	TTC Phe	ACT Thr	GTA Val	GCT Ala	GCA Ala 480	TCT Ser	ACT Thr	GTC Val	TTG Leu	GCC Ala 485	2635
	ACA Thr														AGA '	2683
AAA Lys	ATG Met	AGG Arg	TGG Trp 505	CTG Leu	CTG Leu	GTA Val	TCA Ser	GGG Gly 510	GCA Ala	CCT Pro	AAA Lys	TTC Phe	ATC Ile 515	ATT Ile	CCA Pro	2731
ATT	TGC Cys	ACA Thr 520	ATG Met	ATT Ile	CAA Gln	CTG Leu	ATT Ile 525	CTC Leu	TGT Cys	GGA Gly	ATT Ile	TGG Trp 530	CTG Leu	GGT Gly	ACT Thr	2779
TCT Ser	CCT Pro	CCA Pro	TTT Phe	GTT Val	GAT Asp	GCT Ala	GAT Asp	GGA Gly	CAT His	GTT Val	GAA Glu	AAA Lys	GGC Gly	CAC His	ATT Ile.	2827

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	535					540					545					
														GTC Val		2875
GGA Gly	TAC Tyr	TTA Leu	GTC Val	TCC Ser 570	ATT Ile	GCC Ala	ATT Ile	GCA Ala	AGT Ser 575	TTC Phe	ACC Thr	CTT Leu	GCA Ala	TTC Phe 580	TTC Phe	2923
GCC Ala	AGA Arg	AAT Asn	CTG Leu 585	CCC Pro	GAC Asp	ACA Thr	TTC Phe	AAT Asn 590	GAA Glu	GCC Ala	AAG Lys	TTC Phe	CTA Leu 595	ACA Thr	TTC Phe	2971
														GTC Val		3019
														TGT Cys		3067
TTG Leu 630	GCC Ala	TCT Ser	AGT Ser	GCA Ala	GGG Gly 635	CTG Leu	CTT Leu	TTT Phe	TGC Cys	ATC Ile 640	TTT Phe	GCA Ala	CCA Pro	AAG Lys	TGC Cys 645	3115
														TTT Phe 660		3163
			TCT Ser 665			TAAI	AACA:	TTC 1	ATTA	AATT:	rt to	CTGA	CACA	C TTC	ECTAGA	3219
CATO	GAA'	TTT (STTC	CAA!	ra ai	AGAA	AGGAZ	A GC	ACTA	rgta	TTA	TAAE	TA I	AAAA	rccaaa Cacgtc rtgctg	3279 3339 3399
															rgagtt	3459
TTAT	rgaa?	TA A	TTTC	TAAT	CT T	CACT	rrcc:	r TG	SAAA	TAAA	GTC:	CAGTO	TG :	rg tt (STTGTG	3519
CTCT	LATAI	ATA A	LATA	ATTA:	rg ac	LATAE	AATG	C AA	\AAA/	AAAA	AAA	LAAA	AAA A	LAAAA	AAAA	3578

(2) INFORMATION FOR SEQ ID NO:38:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 667 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Met Ala Pro Lys Asp Thr Ser Leu Ala Leu Ala Met Val Ser Leu Phe 10 Val His Phe Ser Trp Asn Trp Val Gly Ala Val Val Ser Asp Asp 25 Pro Gly Tyr Glu Phe Ile Leu Glu Leu Arg Arg Glu Met Gln Arg Asn 40 45 Asn Phe Cys Leu Ala Phe Val Ser Ile Ile Val Ser Asp Asn Leu Phe Leu Lys Arg Tyr Asn Ile Tyr Tyr Asn Gln Ile Lys Met Ser Ser 70 75 Ala Lys Val Val Ile Ile Tyr Gly Asp Lys Asp Ser Pro Leu Gln Val .

Asn Phe Arg Leu Trp Asn Leu Phe Asp Ile Gln Arg Ile Trp Val Thr Thr Ser Gln Trp Asp Met Ile Ile Asn Asn Gly Lys Phe Leu Leu Asn 125. Ser Phe Tyr Gly Thr Leu Ser Phe Ser His His Tyr Ser Glu Leu Ser Gly Phe Lys Thr Phe Ile Gln Thr Ala Tyr Pro Ser Asn Tyr Ser Asp Asp Phe Ser Leu Gly Ile Leu Trp Trp Val Tyr Phe Asn Cys Ser Leu Ser Leu Ser Glu Cys Lys Asn Leu Gln Asn Cys Pro Lys Glu Asn Ile Phe Arg Trp Leu Tyr Arg His His Phe Glu Met Ser Leu Ser Asp Thr Thr Tyr Asp Leu Tyr Asn Ser Met Tyr Ala Val Ala Tyr Thr Leu Gln Gln Met Leu Lys Gln Ala Asp Thr Trp Gln Ile Asp Asp Gly Lys Glu Pro Glu Phe Asp Ser Trp Gln Met Leu Ser Phe Leu Arg Asn Ile Gln Phe Ile Asn Pro Val Gly Asp Lys Val Asn Leu Asn His Glu Glu Lys Leu Asp Thr Lys Tyr Glu Ile His Gln Thr Leu Thr Phe Leu Pro Asn Pro Val Phe Lys Leu Lys Ile Gly Thr Phe Ser Gln Asn Leu Ser His Gly Arg Gln Leu Tyr Met Leu Lys Glu Met Ile Glu Trp Asn Thr Gly His Gln Gln Ser Pro Thr Ser Val Cys Ser Ile Pro Cys Ser Pro Gly Phe Arg Lys Ser Pro Gln Leu Gly Lys Pro Val Cys Cys Phe Asp Cys Thr Pro Cys Pro Glu Asn Glu Ile Ser Asn Met Thr Asn Met Asn Gln Cys Ile Lys Cys Leu Asn Asp Gln Tyr Ala Asn Pro Gly Gly Thr Arg Cys Leu Lys Lys Val Ile Val Phe Leu Gly Tyr Glu Asp Pro Leu Gly Met Ser Leu Ala Ile Leu Ala Leu Cys Phe Ser Ala Leu Thr Ala Phe Val Leu Ser Ile Phe Leu Lys His Gln Glu Thr Pro Thr Val Lys Ala Asn Asn Arg Thr Leu Ser Tyr Val Leu Leu Ile Ser Leu Ile Ser Cys Phe Leu Cys Ser Leu Leu Phe Ile Gly His Pro Ser Phe Thr Thr Cys Ile Met Gln Gln Thr Thr Phe Ala Val Val Phe Thr Val Ala Ala Ser Thr Val Leu Ala Lys Thr Ile Ile Val Ile Leu Ala Phe Lys Val 485 490 495 Thr Asn Thr Ser Arg Lys Met Arg Trp Leu Leu Val Ser Gly Ala Pro Lys Phe Ile Ile Pro Ile Cys Thr Met Ile Gln Leu Ile Leu Cys Gly Ile Trp Leu Gly Thr Ser Pro Pro Phe Val Asp Ala Asp Gly His Val Glu Lys Gly His Ile Leu Ile Phe Cys Asn Lys Gly Ser Ile Leu Ala Phe Tyr Cys Val Leu Gly Tyr Leu Val Ser Ile Ala Ile Ala Ser Phe Thr Leu Ala Phe Phe Ala Arg Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu Val Phe Cys Ser Val Trp Val Thr

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Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys Ser Met Val Ala Val 615 610

Glu Val Phe Cys Ile Leu Ala Ser Ser Ala Gly Leu Leu Phe Cys Ile 625 630 635 Phe Ala Pro Lys Cys Phe Ile Ile Leu Leu Arg Pro Glu Lys Lys Ser 645 650 655

Phe Gln Lys Phe Gln Asn Ile His Ser Lys Ile 660

(2) INFORMATION FOR SEQ ID NO:39:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 4467 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence (B) LOCATION: 126...2723

 - (D) OTHER INFORMATION: GOVN4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CAGGGATGAG GAAACACCTG TAGAAAAGGA AACCTGAATA CAGGTATAGC ATCTTCTTGG CCAGTGTAGA AGATGGGGAT AATTGCTACC TGTTTGCTGA TCTGTGCAGC AATTAACTAC CAATA ATG TCC AGG CTC AGA GCA GGA AAA AAT ATG CTC ACC TTC ATT TTA Met Ser Arg Leu Arg Ala Gly Lys Asn Met Leu Thr Phe Ile Leu 1 5 10 15												60 120 170			
													ATT Ile 30		218
													AGA Arg		266
													CCT Pro		314
													ACT Thr		362
													ATC Ile		410
													TTC Phe 110		458
													TAA Asn		506
													AAA Lys		554

			GGA Gly													602
			ATA Ile													650
			GGA Gly													698
			TAT Tyr 195													746
			TTC Phe													794
			AAT Asn													842
			AAA Lys													890
			AAT Asn													938
			TCA Ser 275													986
			GCT Ala													1034
			GTC Val												AAA Lys	1082
			TTT Phe													1130
CAC His	AGT Ser	GAG Glu	ATT Ile	TCT Ser 340	GGT Gly	TTT Phe	AAA Lys	TAT Tyr	TTT Phe 345	GTT Val	CAG Gln	ACA Thr	TTG Leu	AAC Asn 350	CCT Pro	1178
			TCA Ser 355													1226
			ATC Ile													1274
			TCA Ser													1322
ATT	ATT	GAA	GGG	AGT	TAT	GAA	ATA	TAC	AAT	GCT	GTG	TAT	GCT	TTT	GCC	1370

Ile 400	Ile	Glu	Gly	Ser	Tyr 405	Glu	Ile	Tyr	Asn	Ala 410	Val	Tyr	Ala	Phe	Ala 415	
					ATG Met											1418
					CAA Gln											1466
					TTC Phe											1514
					CTG Leu											1562
					CTT Leu 485											1610
					GGT Gly											1658
					CGT Arg											1706
					TTT Phe											1754
					AGT Ser											1802
					TGT Cys 565											1850
					TGC Cys											1898
					ATG Met											1946
					ĠTT Val											1994
					AAT Asn											2042
					TTC Phe 645											2090
					ATC Ile										TTC Phe .	2138

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				660					665					670		
														ATT Ile		2186
														CTT Leu		2234
							Ile							CAA Gln		2282
								_						GAT Asp		2330
														AAG Lys 750		2378
-														CTG Leu		2426
														GTC Val		2474
														TGC Cys		2522
														AAG Lys		2570
														GGA Gly 830		2618
														AGA Arg	CCA Pro	2666
													Ser	CAT His		2714
	ATT Ile 865			agtc'	TGA (CTGA	CACA	GG C	ATTG	TTGG	т тс	ATAA	TCAC	CAA	ATATTC	2772
CATT	י א ריי איז		CC N TT	አ ጥረ-ጥ	אתי ידי	الا ملامليان	ሮአ አጥ/	מ אמי	ייריירי ייריירי	አ ሮምሮ	THE CO	ርር ጥጥ	ጥር አ	ጥር እጥ	ATTGCG	2832
															TTCTAC	2892
ATC	AATC	CTA (CTCT'	TTTA	GA G	AAAG	AGAT.	A AT	AGAA'	TTTT	AAA	CATT	TTC .	AGAA'	TTAGAG	2952
															ATCAGG	3012 3072
															TATGAA ATCAGA	3072
															ACACAC	3192
ACA	CACA	CAC :	ACAA	ACAC	AC A	CACA	ATAA	CAA	ATTC	CATA	AAA	TTTT	AAA	AATA	TAGAAT	3252
															CTTACA TAAGAA	3312 3372
															CACTAC	3432

TTGTTGAAAT	AATCTCCATC	TGTGGAATTT	ATAGGGTTTT	GTGACAAAGA	TCAGTTCTGA	3492
TATCAGAGAG	TAAACTGAAG	CAGGCAACCA	TTAGTTGTCA	GCACTGACAG	CAGCTAATGG	3552
AGGTTGCTTC	AGAAATCAAT	TGAGGTTGAT	TCTGGCAATG	AGCAGTTAGA	GAAGATAAAA	3612
AACAGGGAAA	TCAAATATTC	ACACACACAC	ACACACACAC	ACGTACACTC	ACATGCACAA	3672
GCAAGTGCAT	GCATGCAAAC	CCACACAGAC	TACTTGAAGC	AAAGGCAAGG	TCCAGCCACT	3732
TGAAACATAC	AAATGTGTAC	ATATAGACAG	ACACAGACAA	ACACATACAT	ATCCACATGT	3792
TAAATGGCTG	GAGCAATGTC	AGCCAGCAGG	CTCCATGTAT	TTCACATATG	TACATATATG	3852
CATGTAAATA	AATATTCAGA	TATACACATA	TTCACATGTA	CTGGTGGGTA	GGTGGAATAA	3912
AGTTCCAAAA	AACAGGCCCC	AGGAATTTTA	CACATAATGT	ACAGACATAT	ATAACACTAT	3972
TGGTGGAAGA	ACAAGCTCCA	ACATATTCAG	GGAAGCATTG	CATATACATA	CATATAGATT	4032
TGATGGATGG	AACAAAGTTC	CAACAAATTC	TCACATGAAC	TTTATATATG	TATATACATG	4092
AAAGGCAGCC	TGGTTCCCAG	TTGATCAGAG	GTTTGAAAGC	CCAGTGACCC	TAAAAAAGAT	, 4152
GGTAGCCATT	TAGCCTGATT	CCCAGTAAAC	CAGGCAAGTC	ACTAGCCACA	GCCCTCCATA	4212
GAATTTTGGC	CATCAGTCAC	TTAAGCCCAA	CACCCTCCAC	AGATTAAAGG	AAGTGATTAC	4272
AGGTCACAGG	GACTCAGAAC	ACATTTCCAT	TATGTGACAT	AGTCAAAGAC	TTGGAGACTT	4332
AGCCAATGAA	CTTTCCTTCC	CTGAAACTCC	TCCCTGCAGG	CCAACCTTGA	AAAGAGGGGT	4392
ATGGTTTTAC	TCATCTGCTT	TCAGCCATGA	CAATAAATGA	CTTAAAACAA	TGAAAAAAA	4452
АААААААА	AAAAA					4467

(2) INFORMATION FOR SEQ ID NO:40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 866 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Met Ser Arg Leu Arg Ala Gly Lys Asn Met Leu Thr Phe Ile Leu Leu 10 Phe Phe Leu Leu Asn Ile Pro Leu Phe Val Pro Ser Phe Ile Tyr Pro 20 25 Arg Cys Phe Trp Ser Met Lys Lys Asn Glu Tyr Gln Asp Arg Asn Leu 35 40 45 Gly Thr Gly Cys Met Phe Phe Ile Leu Ala Val Gln Gln Pro Met Glu 50 · 55 Lys Glu Tyr Phe Ser His Ile Ser Asn Ile Gln Thr Pro Thr Glu Asn 70 75 Gln Lys Tyr Pro Leu Thr Leu Ala Phe Ser Met Asn Glu Ile Asn Asn 90 85 Asn Pro Asp Leu Leu Pro Asn Met Ser Leu Ala Phe Thr Phe Ser Glu 100 105 Tyr Ser Cys Tyr Leu Glu Ser His His Lys Arg Leu Phe Asn Phe Ser 115 120 125 Leu Lys Asn His Glu Ile Leu Pro Asn Phe Ile Cys Thr Lys Asp Ile 130 135 140 Lys Cys Gly Val Val Leu Thr Gly Leu Ser Leu Val Thr Thr Val Thr 150 155 160 Leu His Ile Ile Leu Asn Asn Phe Ile Phe Gln Gln Phe Arg Gln Leu 165 170 Thr Tyr Gly His Phe His Pro Ala Leu Cys Asp His Glu Asn Phe Pro 180 185 His Leu Tyr Gln Met Ala Ser Asp Asp Thr Ser Leu Ala Leu Ala Leu 195 200 205 Val Ser Phe Ile Ile His Phe Ser Trp Asn Trp Ile Gly Leu Ala Ile 215 220 Ser Asp Asn Asp Gln Gly Ile His Phe Leu Ser Tyr Leu Arg Arg Glu 230 235 Met Glu Lys Asn Thr Val Cys Phe Ala Phe Val Asn Ile Ile Pro Val 245 250 Asn Met Asn Leu Tyr Met Ser Arg Ala Glu Val Tyr Tyr Ser Gln Val .

			260					265					270		
Met	Thr	Ser 275	Ser	Ala	Asn	Val	Val 280	Ile	Ile	Tyr	Gly	Asp 285	Thr	Gly	Asn
Thr	Leu 290	Ala	Val	Ser	Phe	Arg 295	Met	Trp	Asp	Ser	Leu 300	Gly	Ile	Gln	Arg
Leu 305	Trp	Val	Thr	Thr	Ser 310	Gln	Trp	Asp	Val	Thr 315	Pro	Phe	Lys	Lys	Asp 320
Phe	Thr	Phe	Asp	Asn 325	Gly	Tyr	Gly	Thr	Phe 330	Gly	Phe	Gly	His	Arg 335	His
Ser	Glu	Ile	Ser 340	Gly	Phe	Lys	Tyr	Phe 345	Val	Gln	Thr	Leu	Asn 350	Pro	Phe
Lys	Tyr	Ser 355	Asp	Glu	Tyr	Leu	Val 360	Lys	Leu	Glu	Trp	Met 365	Tyr	Val	Asn
	370				Tyr	375	_	_			380		-		
Asn 385	His	Ser	Leu	Glu	Trp 390	Leu	Met	Thr	His	Thr 395	Phe	Asp	Met	Ala	Ile 400
		_		405	Glu		_		410		_			415	
			420		Thr			425					430		
	•	435			Asn	-	440	•	-			445			
	450				Thr	455				-	460				
465					Lys 470					475					480
				485	Gly				490		-			495	
_			500		Gln		•	505					510		
		515			Ile		520					525			
	530				Arg	535					540				
545		_	-		Pro 550	_				555					560
				565	Val				570					575	
			580		Ile			585					590		
		595	•		Ala		600					605			
	610				Leu	615					620				
625		_			Asn 630	_				635	•				640
				645	Leu				650					655	
_			660					665					670		
		675			Val Pro		680	_				685			
	690					695					700				
705					Ile 710 Leu					715					720
				725	Gly				730					735	
			740		Cys			745			_		750		
		755			Ala		760					765			
	770	FIIG	TILL	Tea	A1 d	775	neu	96 <u>1</u>	AL 9	von	780	LTO	val	1111	E 116

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Asn 785	Glu	Ala	Lys	Ser	Met 790	Thr	Phe	Ser	Met	Leu 795	Val	Phe	Суз	Ser	
	Val	Thr	Phe			Val	Tyr	His	-		Lys	Gly	Lys	Val	800 Met
Val	Ala	Val	Glu	805 Ile	Phe	Ser	Thr	Leu	810 Ala	Ser	Ser	Ala	Gly	815 Met	Leu
Gly	Cys	Ile	820 Phe	Ala	Pro	Lys	Cys	825 Tyr	Thr	Ile	Leu	Phe	830 Arg	Pro	Asp
		835					840	_				845	_	Thr	_
	850					855	3		-,-		860	-		****	
865	Leu														

(2) INFORMATION FOR SEQ ID NO:41:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2916 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence (B) LOCATION: 299...2635

 - (D) OTHER INFORMATION: GOVN5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

CGGCACGAGT TCAACTAGTC ATGTTCAAGA AGGGGCAAAT ACTTTGTTAA TATGCTCTTC	60
GCTTGGACTT TTATCTCTTG CTTTCTGCAG ATTCCAATTA TTTTATGCTC CTACAGAAGC	120
AGCGAGTGCT TAGTCAAGAT GAATTATCGT TTAAAGGGGA AAGGAAATGT GGTGATTGTT	180
GGATTTTTCC CTGCTTTTGC TGTCTACCCC CTCAACAAAA CAATTGACTG GTGGATGCTT	240
AAATTCAGCA AAGAATTATG ATTGAGTTTA AGTTGAAGAG CTACCAGTAT ATTTGGCC AT	300
Met .	
1	
CAG COMP TOO CAT TOO CAN AND CAN AND CAN	
GAG GTT TGC CAT TGA GGA AAT CAA CAG CAA TCC CCA TCT TTT ACC AAA	348
Arg Phe Ala Ile Glu Glu Ile Asn Ser Asn Pro His Leu Leu Pro Asn	
5 10 15	
CAC ATC CCT GGG ATT TGA GAT CAA TAA TGT CCC ACA CGG TCA GAG GTA	396
Thr Ser Leu Gly Phe Glu Ile Asn Asn Val Pro His Gly Gln Arg Tyr	396
20 25 30	
25 25	
CAC TCT GGT CAA ACT TTT TAG CTC ACT TTC AGG GTC TAA TTA TGA CAT	444
Thr Leu Val Lys Leu Phe Ser Ser Leu Ser Gly Ser Asn Tyr Asp Ile	
35 40 45	
TCC TAA CTA CAT AAG TGC AAG TGA GAG CAA TTC TGC TGC TGT ACT TAC	492
Pro Asn Tyr Ile Ser Ala Ser Glu Ser Asn Ser Ala Ala Val Leu Thr	
50 55 60 65	
AGG ACC ATC GTG GAC AAT ATC TGA ATG CGT AGG GAC ACT CCT GGA TCT	540
Gly Pro Ser Trp Thr Ile Ser Glu Cys Val Gly Thr Leu Leu Asp Leu	
70 75 80	
TTA CAA AUT DOG ACA COU DAG DOG DOG COO DEED DOG COO DE DOG COO DE DOG COO DE DOG COO DEED DOG COO DEED DOG C	
TTA CAA ATT TCC ACA GCT TAC TTT TGG GCC TTT TGA TAG TCT CCT GAG Tyr Lys Phe Pro Gln Leu Thr Phe Gly Pro Phe Asp Ser Leu Leu Ser	588
85 90 95	
TGA ACA AAG ACG GTT TTC TTC TCT GTA CCA AGT GGC CCC CAA AGA TAC	636
Glu Gln Arg Arg Phe Ser Ser Leu Tyr Gln Val Ala Pro Lys Asp Thr.	020

110

105

100

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ATT TCT GAC GCC TGG CAT TGT ATC TTT GAT GCT TCA TTT CCA CTG GAA Phe Leu Thr Pro Gly Ile Val Ser Leu Met Leu His Phe His Trp Asn 115 120 125	684
CTG GGT GGG GTT ATT CAT CAT AGA TGA TGA CAA AGG TGC CCA GAC ACT Trp Val Gly Leu Phe Ile Ile Asp Asp Asp Lys Gly Ala Gln Thr Leu 130 140 14	732
GTC AGA CTT GAG AAA TGA GAT GGA TAA AAA TGG AGT CTG CAC AGC ATT Ser Asp Leu Arg Asn Glu Met Asp Lys Asn Gly Val Cys Thr Ala Phe 150 155 160	780
TGT AGA AAT GAT CCC AGT CAT CAA GGG TTC ATT TTT TAC CAA ATC CTG Val Glu Met Ile Pro Val Ile Lys Gly Ser Phe Phe Thr Lys Ser Trp 165 170 175	828
GAA AAA TCA TGT GCA GAT CCT GGA ATC ATC ATC AAA TGT GAT TAT TAT Lys Asn His Val Gln Ile Leu Glu Ser Ser Asn Val Ile Ile 180 180	876
TTA TGG GGA CTC TGA TTC TCT ATT AAG CTT AAT AGT AAA TAT TAA GCA Tyr Gly Asp Ser Asp Ser Leu Leu Ser Leu Ile Val Asn Ile Lys Gln 195 200 205	924
GAA GTT GCT CAC ATG GAA AGT GTG GGT ACT GAT CTC ACA GTG GGA TGT Lys Leu Leu Thr Trp Lys Val Trp Val Leu Ile Ser Gln Trp Asp Val 210 220 22	972
TTC TAA ATT TGA TGA TTA TTT CAT GGT AGA CTC ATT GCA TGG AGC TCT Ser Lys Phe Asp Asp Tyr Phe Met Val Asp Ser Leu His Gly Ala Leu 230 235 240	1020
TAT TTT TTC ACA CCA TCG TGA GGA GAT TCC TAA TTT TAC AGA TTT TAT Ile Phe Ser His His Arg Glu Glu Ile Pro Asn Phe Thr Asp Phe Met 245 250 255	1068
GCA GAA GTA CAA CCC TTC CAA GTA CCC GGA AGA CAC TTA TCT TCA TGT Gln Lys Tyr Asn Pro Ser Lys Tyr Pro Glu Asp Thr Tyr Leu His Val 260 265 270	1116
ATT GTG GCA CAT GTA CTT CAA TTG CTC ATT TGT TAA GAA AGA TTG TAA Leu Trp His Met Tyr Phe Asn Cys Ser Phe Val Lys Lys Asp Cys Lys 275 280 285	1164
AAT TGT GCA CAA CTG TTT GCC TAA TGC CTC CCT GGG GTT CTT GCC TGG Ile Val His Asn Cys Leu Pro Asn Ala Ser Leu Gly Phe Leu Pro Gly 290 295 300 30	1212
GAA CAT ATT TGA CAT GGC CAT GAG TGA AGA GAG TTA CAA TGT ATA CAA Asn Ile Phe Asp Met Ala Met Ser Glu Glu Ser Tyr Asn Val Tyr Asn 310 315 320	1260
TGC TGT GTA TGC TGT GGC CCA CAG TCT GCA TGA GAT GAT TCT CAA CCA Ala Val Tyr Ala Val Ala His Ser Leu His Glu Met Ile Leu Asn Gln 325 330 335	1308
AGT ACA ATT TCA AAC TCA TGA AAA AGG AAA AAA GAT GGT ATT CTT TCC Val Gln Phe Gln Thr His Glu Lys Gly Lys Met Val Phe Phe Pro 340 345 350	1356
TTG GCA GCT TCA CCC CTT TCT AAG GGA AAG ACA ACT CAT CAA TCA GAA Trp Gln Leu His Pro Phe Leu Arg Glu Arg Gln Leu Ile Asn Gln Asn 355 360 365	1404

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•	TGG AGC Gly Ala 370												1452
5	TGA CAT Asp Ile			Trp A								n Val	1500
1	GAA AGT Lys Val	. Gly '								in L			1548
	CAT ATC Ile Ser	Ser 2	Asn Met	: Ile G	ln Tri 425	Ala 5	Thr	Gly	Ser 1	Thr G	lu Ile	e Pro	1596
	ACA GTC Gln Ser 435	Val		Glu S				Gly					1644
	CCA GGA Gln Glu 450	Gly .	Arg Val	455	ув Сув	s Phe	Asp	Cys 460	Ile I	Pro C	ys Pro	o Glu 46	1692
5	AAA TGA Asn Gli			n Glu I								s Pro	1740
	AGA AAC Glu Thi	His	Tyr Ala 485	a Asn I	le Glu	1 Lys 490	Ile	His	Cys I	Leu G .4	ln Ly: 95	s Thr	1788
	TGT GAC Val Thi					Pro			Lys 7	_		_	1836
	CAT GTC Met Sei 51:	Leu		e Ser S							_		1884
	TCT GAA Leu Lys 530										_		1932
5	CAG TTA Ser Tyi	Thr	Leu Lei 55	ı Ile T	hr Le	u Met	Leu 555	Сув	Phe 1	Leu C	ys Pro 56	o Leu O	1980
	GCT CTT Leu Phe	e Ile					Ser			Leu G			2028
	CAT TTT Ile Phe					l Ala			Thr '				2076
	AAC TAT Thr Ile 59!	e Thr		l Ile A									
	TAG AAG Arg Arg 610												2172
	ATG CAC	CCT G	CT CCA	AGT T	T TCT	ATC	TGG 2	TAA	rtg g	CT GA	C AAC	CTC .	2220

5	Cys	Thr	Leu	Leu	Gln 630	Val	Phe	Leu	Ser	Gly 635	Ile	Trp	Leu	Thr	Thr 640	Ser	
•				TAT T Ile 645													2268
•			-	CAA 7 Asn													2316
1			Gly	AGC A Ala						-			Ala				2364
(Asn		ACC T								Phe					2412
5				GTT (Phe													2460
•				GGG (Gly 725						Met							2508
(TAC I					Ile								2556
(Leu	ATT) Leu									Tyr		-		2604
•		Thr		TGC : Ala								GCAT	CCTT	ATG	rgcc	TCT T	2656
	AAGT CCTA FATT	CATA ATGC AGTT	AT T TT T	GTACI TTTCI	ATTTO ACAT ATTG	G AT T AA A TT	CCAG AATA	GGC TGTG	TAT CTG	TATT CATT	TCT TTT	TTAG CGTC	TAGT TTCC	CA T. TC T	ATAT. TCTA	ATATA ATGTA CTTAC TCCAA	2716 2776 2836 2896 2916
			(-1								_						

(2) INFORMATION FOR SEQ ID NO:42:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 779 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

Met Arg Phe Ala Ile Glu Glu Ile Asn Ser Asn Pro His Leu Leu Pro 10 Asn Thr Ser Leu Gly Phe Glu Ile Asn Asn Val Pro His Gly Gln Arg 20 25 Tyr Thr Leu Val Lys Leu Phe Ser Ser Leu Ser Gly Ser Asn Tyr Asp 40 45 Ile Pro Asn Tyr Ile Ser Ala Ser Glu Ser Asn Ser Ala Ala Val Leu .

Thr Gly Pro Ser Trp Thr Ile Ser Glu Cys Val Gly Thr Leu Leu Asp Leu Tyr Lys Phe Pro Gln Leu Thr Phe Gly Pro Phe Asp Ser Leu Leu Ser Glu Gln Arg Arg Phe Ser Ser Leu Tyr Gln Val Ala Pro Lys Asp Thr Phe Leu Thr Pro Gly Ile Val Ser Leu Met Leu His Phe His Trp Asn Trp Val Gly Leu Phe Ile Ile Asp Asp Asp Lys Gly Ala Gln Thr Leu Ser Asp Leu Arg Asn Glu Met Asp Lys Asn Gly Val Cys Thr Ala Phe Val Glu Met Ile Pro Val Ile Lys Gly Ser Phe Phe Thr Lys Ser Trp Lys Asn His Val Gln Ile Leu Glu Ser Ser Asn Val Ile Ile Ile Tyr Gly Asp Ser Asp Ser Leu Leu Ser Leu Ile Val Asn Ile Lys Gln Lys Leu Leu Thr Trp Lys Val Trp Val Leu Ile Ser Gln Trp Asp Val Ser Lys Phe Asp Asp Tyr Phe Met Val Asp Ser Leu His Gly Ala Leu Ile Phe Ser His His Arg Glu Glu Ile Pro Asn Phe Thr Asp Phe Met Gln Lys Tyr Asn Pro Ser Lys Tyr Pro Glu Asp Thr Tyr Leu His Val Leu Trp His Met Tyr Phe Asn Cys Ser Phe Val Lys Lys Asp Cys Lys Ile Val His Asn Cys Leu Pro Asn Ala Ser Leu Gly Phe Leu Pro Gly Asn Ile Phe Asp Met Ala Met Ser Glu Glu Ser Tyr Asn Val Tyr Asn Ala Val Tyr Ala Val Ala His Ser Leu His Glu Met Ile Leu Asn Gln Val Gln Phe Gln Thr His Glu Lys Gly Lys Lys Met Val Phe Phe Pro Trp Gln Leu His Pro Phe Leu Arg Glu Arg Gln Leu Ile Asn Gln Asn Gly Ala Asn Glu Asp Leu Asp Cys Thr Arg Lys Ser His Val Glu Tyr Asp Ile Leu Asn Phe Trp Asn Phe Pro Lys Gly Leu Gly Leu Asn Val Lys Val Gly Thr Phe Ser Pro Ser Ala Pro Lys Glu Gln Lys Leu Ser Ile Ser Ser Asn Met Ile Gln Trp Ala Thr Gly Ser Thr Glu Ile Pro Gln Ser Val Cys Ser Glu Ser Cys His Pro Gly Phe Arg Lys Thr His Gln Glu Gly Arg Val Ala Cys Cys Phe Asp Cys Ile Pro Cys Pro Glu Asn Glu Ile Ser Asn Glu Thr Asp Val Asp Gln Cys Val Lys Cys Pro Glu Thr His Tyr Ala Asn Ile Glu Lys Ile His Cys Leu Gln Lys Thr Val Thr Phe Leu Tyr Tyr Asp Asp Pro Leu Gly Lys Thr Leu Cys Phe Met Ser Leu Gly Phe Ser Ser Leu Thr Ala Ala Val Leu Val Val Phe Leu Lys Asn Arg Asp Thr Pro Ile Val Lys Ala Asn Asn Leu Ala Leu Ser Tyr Thr Leu Leu Ile Thr Leu Met Leu Cys Phe Leu Cys Pro Leu Leu Phe Ile Gly Arg Pro Ser Thr Ala Ser Cys Ile Leu Gln Gln

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Asn Ile Phe Gly Leu Leu Phe Thr Val Ala Leu Ser Thr Val Leu Ala 580 585 Lys Thr Ile Thr Val Val Ile Ala Phe Lys Ile Thr Ser Pro Gly Arg 600 595 605 Ile Arg Arg Trp Leu Leu Ile Ser Arg Ala Pro Asn Phe Ile Ile Pro 610 615 620 Leu Cys Thr Leu Leu Gln Val Phe Leu Ser Gly Ile Trp Leu Thr Thr 630 635 Ser Pro Pro Phe Ile Asp Lys Asp Ala His Ser Glu His Gly His Ile 645 650 Ile Ile Ile Cys Asn Lys Gly Ser Ala Val Ala Phe His Cys Asn Leu 660 665 Gly Tyr Leu Gly Ala Leu Ala Leu Val Ser Tyr Phe Met Ala Phe Leu 680 Ser Arg Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu Ala Phe 695 Ser Met Leu Val Phe Cys Ser Val Trp Val Thr Phe Leu Pro Val Tyr 710 715 720 His Ser Thr Lys Gly Lys Asn Met Val Ala Met Glu Val Phe Ser Ile 725 730 735 Leu Ala Ser Ser Thr Ser Leu Leu Gly Ile Ile Phe Ala Pro Lys Cys 740 745 750 Tyr Leu Ile Leu Leu Arg Pro Glu Arg Asn Ser Leu Ser Tyr Ile Arg 755 760 Asp Lys Thr Tyr Ala Lys Ser Ile Lys Pro Ser 775

(2) INFORMATION FOR SEQ ID NO:43:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3307 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 112...1761
 - (D) OTHER INFORMATION: GOVN6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

 	ATC	TTCCAC F AAG Lys	60 117						
		 	 	_	 		GAA Glu		165
		Glu					AAT Asn		213
				 			TTT Phe		261
							TCT Ser 65		309

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																	_
	_					TTG Leu	_										357
						AAT Asn											405
						ACT Thr											453
7						AGT Ser 120											501
						AAG Lys											549
						AAG Lys											597
						CAA Gln											645
						TTT Phe											693
1						AAA Lys 200											741
						ATT Ile											789
						ATG Met											837
						ATG Met											885
						GGG Gly											933
נ						AAT Asn 280											981
						GTA Val								_		-	1029
						TGT Cys											1077
7	CA	TTG	GAA	TGG	TTA	ATG	GAG	CAG	ACA	TTT	GAC	ATG	GTC	TTT	AGT	GAT	1125

Ser Le	u Glu 325	_	Leu	Met		Gln 330	Thr	Phe	Asp	Met	Val 335	Phe	Ser	Asp	
GGA AG Gly Se 34	r Arg														1173
CAT GA His Gl 355															1221
AAA GG Lys Gl															1269
ACC CA Thr Hi															1317
GAA AT Glu Il		Gln													1365
CAG CA Gln Hi 42	s Ile														1413
CCA CA Pro Hi 435															1461
ACA GG Thr Gl								_							1509
CCT GG Pro Gl															1557
GTT TG Val Cy		Pro													1605
GAT CA Asp Gl 50	n Cys														1653
GAC AA Asp Ly 515															1701
CTT GG Leu Gl															1749
AGC TG Ser Cy			TAG	ggtc:	PTT (GTGA	AGCA	CC A'	TGAC	ACTC(C TA	r t gt(GAAG	GCCAA	1806
TGTATT CAAAGT CATTAT	CATT CACT CACA CCCC	GGCC GTGG AACC ATAT	ATCC CTAT CAGG GTTC	TA AC TT C' AA GI CC TC	CAGA FACA AAGG' GTTT	GCAA ATTT TTGA CAAT	C CTO T GGO G AA G TA	GCAT CAAA ACTT TTCT	CTTA AACA CCTA GTGT	CAG ATC GTA GCA	CAAA' ACTG' ITGG(ATCT(TCA (TGG ' GTA (GGC '	CATT TTCT CACT TAGC	CTCATT IGGAAT GGCTTT CAACTA AGTTTC GTGCAA	1866 1926 1986 2046 2106 2166

CAAAGGCTCA GTAACTGCAT TCTACTGTGT CCTGGGATAC TTGGCCTGCT TGGCACTTGC 2226 AAGCTTCACT GTGGCTTTCT TGGCAAAGAA TCTGCCAGAC ACATTCAATG AAGCCAAGTT CTTGACCTTC AGCATGCTGG TGTTCTGCAG TGTCTGGGTC ACCTTCCTCC CTGTCTACCA CAGCACCAAG GGCAAGATCA TGGTTGCTGT GGAGATATTC TCCATTTTGG CATCCAGTGC 2406 AGGGATGCTT GGATGCATCT TTGCACCCAA GATTTACATC ATTTTAATGA GACCAGAGAG 2466 AAATGCTATC CAAAAGATCA GGGAGAAATC ATATTTCTGA ACAAATTATT TCAGAATTTC 2526 TATCAAATGT AAACATGGTA TATACCCATC AAATATTGTG TTACAGTGCA TGTATCTAGT TTTAGAATCA CTCTCACTGG TACCCCTAGT GATGTCTAGA AATATCATAT CTACCAATCT 2646 TGAATACATT GTCCATAAAA TCTTGTACAT ATTCACTAGC TTAGTTTCCT GTGGGAGAAC TAAAATTCTC AAATTATTAT TACAATTTTA TTCATAATTT TGCTCTCATG GCAAATCAGA ACTCATTTTC TAATTTCCAG TAACAACACA TACATGACAG AATACTGATT TTCAGCTATT CTTTAAGCTA TTGGCCAATA GACTAAGGTG GAAATGTTCT TTTTCTTTCT GAAACACAAA 2886 AATATTATAT CATATAATAC ACAGAAGTCA GGGACCCCTA TGGATGAATT AGGGAATAGT TGGAAGAAGC TGGCTGAGTA GAAGGGTGAC CCATAGGAAG ACCAGCAGTC TCACCTAACA AGGACAACCA AGATCTTGCT GACACTGAAT CACTTGCTAG GCAGTTGATT TGAGGCCCCT GACACATATC AAGCATAGGA CTACATTGGC TGGCCTCAGT GGGAGAAGAC AACCTAACCC 3126 CCTAGAGACT TGAGGCCCCA GGCTAAGGGG AGGTTGGGGG TTTTGAAAGT TGGGGATATT 3186 ATCTTGGAGT TGGGGAGGG TATGGGATGA AGAAGAGTCA GGAGGCAGGT GCTGGTTGGA 3246 GTATAATGAC TGGACTGTAA ATAAAAGACT AACAACCAAA AATAAATAAA ATAACTTAAA 3306 3307

(2) INFORMATION FOR SEQ ID NO:44:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 550 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Met Lys Leu Arg Asp Lys Asp Leu Ser Ile Thr Cys Ser Phe Ile Leu 10 Glu Ala Val Gln Met Pro Thr Glu Asn Asp Tyr Phe Asn Gln Thr Leu 20 25 30 Asn Ile Leu Lys Thr Thr Lys Asn His Lys Tyr Ala Leu Ala Leu Ala 35 40 Phe Ser Ile Asp Glu Ile Asn Arg Asn Pro Asp Leu Leu Pro Asn Met 55 60 Ser Leu Ile Ile Lys Tyr Pro Leu Gly Leu Cys Asp Gly Gln Thr Thr Leu Pro Thr Pro Tyr Leu Phe Asn Glu Ile Tyr Phe Arg Pro Ile Pro 90 Asn Tyr Phe Cys Asn Glu Glu Thr Met Cys Thr Phe Leu Leu Thr Gly 105 Pro His Trp Ile Thr Ser Tyr Ser Phe Trp Ile His Leu Asn Ile Phe 120 Leu Ser Pro Ser Met Asn Pro Lys Asp Thr Ser Leu Ala Leu Ala Met 135 Val Ser Phe Leu Leu Tyr Phe Lys Trp Asn Trp Val Gly Leu Val Ile 150 155 Ser Asp Asp Gln Gly Asn Gln Phe Leu Ser Glu Leu Lys Lys Glu 170 175 165 Ser Lys Ile Lys Glu Ile Cys Phe Ala Phe Val Ser Met Leu Ala Ile 185 180 Asp Glu Ile Ser Phe Tyr His Lys Thr Glu Met Tyr Tyr Asn Gln Ile 200 205 Val Met Ser Ser Thr Asn Val Ile Ile Ile Tyr Gly Lys Thr Glu Ser 215 210 220 Ile Ile Glu Leu Ser Phe Arg Met Trp Glu Ser Pro Val Ile Gln Arg 230 235 Ile Trp Val Thr Thr Lys Glu Met Asn Phe Pro Thr Ser Lys Arg Asp

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250
               245
Leu Thr His Asp Thr Phe Tyr Gly Thr Leu Thr Phe Leu His Ser His
                    265
         260
                                              270
Gly Glu Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Trp Tyr His Leu
       275
                          280
                                              285
Arg Ile Thr Asp Leu His Leu Val Met Pro Glu Trp Lys Tyr Phe Asn
                     295
                                         300
   290
Tyr Glu Ala Ser Ala Ser Asn Cys Lys Ile Leu Lys Asn Tyr Ser Ser
                  310
                                      315
Ser Ala Ser Leu Glu Trp Leu Met Glu Gln Thr Phe Asp Met Val Phe
                                 330
              325
                                                  335
Ser Asp Gly Ser Arg Asp Ile Tyr Asn Ala Val Asn Ala Met Ala His
                              345
           340
                                                  350
Ala Leu His Glu Met Asn Leu His Leu Val Asp Asn Gln Ala Ile Asp
                           360
                                              365
Asn Gly Lys Gly Ala Ser Ser His Cys Phe Lys Ile Asn Ser Phe Leu
                      375
                                          380
Arg Lys Thr His Phe Thr Asn Pro Leu Gly Asp Arg Val Ile Met Lys
                   390
                                       395
Glu Arg Glu Ile Leu Gln Glu Asp Tyr Asn Ile Phe His Thr Trp Asn
               405
                                  410
Phe Ser Gln His Ile Gly Phe Lys Val Lys Ile Gly Lys Phe Ser Pro
                               425
                                                  430
Tyr Phe Pro His Gly Arg His Phe His Leu Tyr Val Asp Met Ile Glu
                          440
Leu Ala Thr Gly Ser Arg Lys Met Pro Ser Ser Val Cys Thr Glu Asp
   450
                       455
                                          460
Cys Ser Pro Gly Tyr Arg Arg Phe Trp Lys Glu Gly Met Ala Ala Cys
                  470
                                      475
Cys Phe Val Cys Ser Pro Cys Pro Glu Asn Ala Ile Ser Asn Glu Thr
               485
                                   490
Asn Met Asp Gln Cys Val Asn Cys Pro Glu Tyr Gln Tyr Ala Asn Thr
          500
                              505
Lys Arg Asp Lys Cys Ile Gln Lys Asn Val Met Phe Leu Ser Tyr Lys
       515
                          520
                                              525
Asp Pro Leu Gly Asp Asp Ser Cys Leu His Ser Leu Leu Phe Leu Cys
                      535
Ile Asn Ser Cys Cys Thr
```

(2) INFORMATION FOR SEQ ID NO:45:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3938 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 46...2424
 - (D) OTHER INFORMATION: GOVN7
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

CGGCACGAGC CCAGGTTTAA GGCTGGAAAA AATATGTTCA TTTTG ATG ATA GTA TTC Met Ile Val Phe

TTT CTC CTC AAC ATT CCA CTT CTC ATG GCA AAT TCC GTT GAT CCC AGG Phe Leu Leu Asn Ile Pro Leu Leu Met Ala Asn Ser Val Asp Pro Arg 10 15

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								- 1	132 -								-
														TTA Leu 35		i	153
														GAG Glu		;	201
														TAC Tyr		;	249
														AGG Arg			297
														TTG Leu			345
														TTT Phe 115			393
														TCA Ser			441
														ATT Ile			489
														CCT Pro			537
														CAG Gln			585
														ATA Ile 195		•	633
														GAT Asp	GAA Glu		681
															GAA Glu		729
														TCA Ser			777
	Lys					Tyr					Val				GCA Ala 260		825
					Tyr										TGT Cys		873
TTC	AGA	ACA	TGG	ACA	TCT	CCA	GTC	ATA	CAG	AGG	ATA	TGG	GTT	ACC	AAA		921

								•								-
Phe	Arg	Thr	Trp 280	Thr	Ser	Pro	Val	Ile 285	Gln	Arg	Ile	Trp	Val 290	Thr	Lys	
				TTC Phe												969
				CTA Leu												1017
				GTA Val												1065
				CCA Pro 345												1113
				ATA Ile												1161
				CAG Gln												1209
				GCT Ala												1257
				ATT Ile												1305
				TTG Leu 425												1353
				GGG Gly												1401
			Tyr	GAC Asp												1449
				AAG Lys												1497
	Gln			TTA Leu												1545
				TTA Leu 505											Tyr	1593
				AAG Lys					Ala							1641
															TGG	1689

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			_					- 4 -				
	535		5	640				545				
GTC TTT Val Phe 550						Val						1737
	AGC TAC Ser Tyr		Ile M		Leu l							1785
TCC TTT Ser Phe	TTC TTC Phe Phe											1833
CAA ATC Gln Ile	ACA TTT Thr Phe 600											1881
GCC AAA Ala Lys			Leu L									1929
AGA AAG Arg Lys 630						Thr						1977
CCC ATA Pro Ile 645	TGT TCC Cys Ser	CTG TTG Leu Leu 650	Gln C	GC ACT	Leu	TGT Cys 655	GCA Ala	ATT Ile	TGG Trp	CTA Leu	GCA Ala 660	2025
GTT TCT Val Ser	CCA CCA Pro Pro											2073
ATC ATA Ile Ile	ATT GTG Ile Val 680											2121
CTG GGA Leu Gly	TAT TTG Tyr Leu 695		Leu A									2169
TTG GCA Leu Ala 710	AAG AAT Lys Asn					Glu						2217
	ATG CTA Met Leu		Cys S		Trp							2265
TAC CAT Tyr His	AGC ACC											2313
ATT TTG Ile Leu	ACA TCC Thr Ser 760	Ser Ala										2361
ATT TAC Ile Tyr	ATC ATT Ile Ile 775		Lys P									2409
	TCA CGT Ser Arg		ACAGAT	ra tttt	AGAAA	T TC	TGTO	CAAA	r gt <i>i</i>	ACAG:	rtgt t	2465

ATATACCCAC CAAATATTTG GTTACAGTGC ATAAATCTAG TTTTAGAACT CTCACTAGTT CCTCTAATGA TATCTAGAAA TATTGTATCT ACCAATCTTA CATTCATTAT CCATAAAATC CTGCACTCAT TCACTTGTTT GTTCTACTCT GTGAGAAATA TAATTCCCAA TGTAGTATTA 2645 AATTTTTCT AAAAATTTTG CTTTAATTGA CATTTTTCC CTTATAACTT CAAGTACATT TGATAAGGCA TTTGAATCTA TAACCTTTTA TACAATAAGA TCCAGGACAG ACAGGATTAC ACATAGAAAC CGTCTATCGA ATCAAACAAT CAATCAGACT AAAAAACAAA GAATCAACAA AGATAACATC AGAATACATT ATCTGATTTC CAGTAGAAGC ACATATGTGA CAGAATACTG TCTGTTTTTA TAGTTCCTCT TCAAGCTATT GTATTGGTCA GCAGTCTAAG GTAGAAGTTT TTTTGTCACA AACACAAAAA TATTGTATCC AACAATGGAC AGAATCCAGT GAGCACCCTG 3005 TTCAAATTTG GAGATAGTTG GAATATCATG AAAAAGAGGG TGACCCATAA GAATACCAGC ATTCTCAACT AACCTGGACA ACCACGAATT TGAGCTGCTG ACCAGGCAGC ATACATAAGC 3125 TGATATGAGG CTCCCAGCAC AGATGCAACA TAGGGCTGCC TGGTCTGGCC TCAGTGGAAG 3185 AAGACACATT TAAACCACAA GAGACAGGAG TCACAAGGGA TTGGGAAGGT GTGATGGTTT GCATATGCTT GGCTCAGGAA GTGGCACTAT TAGAAGGTGT AGACTTGATG GAGGAATTTG TCACTGTAGG GGTGGGCTTG GAGATCCACC TCATAGCTGC CTGGGGATGC TCAGTCTGTT CCTGGCTTCC TTCAGGTGAA GATATAGAAC TCAGATCCTC CTTCACCAAG CCTGCCTGGA 3425 TGCTGTGATG CTGCCATGCT CCGACCTTGA TGATAATGGA CTGAACCTCT GAACATGTAA GCTGGCTCCA ATTAAAGGTT GTCCTTTATA AAACTTCCAT TGATCACAGT GTCTGTACAT AGCAATAAGA CCCAAACTAA GACAGAAGGT GTGTGGATTG GGGAAGTGGG GATTTCCTCT TGGAGGTGGG GAAGTAGTCA AAGATTAAAT TGGGAAGGGG ATAATGAGTA CACCGTAAAA AGTATTAAAG AATAAAATAC TAAAAAATTA ATTAAATAGG ATTGTGAATA TATTAACATG CTATTATATT ATAGTTCTGG AAGGGATAGG TAAAACTCCT GATGGTGGTT TGTACCTAAT TTTTCTTAGA GCTTGCCCTT TGTATTCAGT TGTGATTGAA ATCCTGGGCT CACAAAATTC TAGTACTATG GATATGGAGG CAGATACTTT GATTACGCTG CTTCCTAGAA ATAAATTTTC 3905 САЛАЛАССАЛ ЛАЛАЛАЛАЛА ЛАЛАЛАЛАЛА АЛА

(2) INFORMATION FOR SEQ ID NO:46:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 793 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEO ID NO:46:

Met Ile Val Phe Phe Leu Leu Asn Ile Pro Leu Leu Met Ala Asn Ser 10 Val Asp Pro Arg Cys Phe Trp Lys Ile Asn Leu Asn Glu Val Lys Asp 20 25 Ile Asp Leu Asp Thr Ser Cys Tyr Phe Ile Leu Glu Ala Val Gln Leu 40 Pro Met Glu Lys Asp Tyr Phe Asn Gln Thr Leu Asn Val Leu Lys Thr 55 Thr Lys Tyr Asn Arg Tyr Ala Leu Ala Leu Ala Phe Thr Met Asp Glu Ile Asn Arg Asn Pro His Ile Leu Pro Asn Met Ser Leu Ile Ile Lys His Thr Leu Gly His Cys Asp Gly Asn Ile Pro Leu Arg Leu Leu Asn 105 Gln Ile Phe Tyr Met Pro Phe Pro Asn Tyr Gly Cys Asn Glu Glu Thr 120 125 Met Cys Ser Phe Met Leu Met Gly Pro Asn Leu Trp Pro Ser Val Asp 135 140 Phe Phe Ile His Leu Asn Ile Leu Phe Pro His Phe Leu Gln Ile Ser 150 155 Phe Gly Pro Phe His Ser Ile Phe Ser Asp Asn Glu Gln Phe Pro Tyr 165 170 Ile Tyr Gln Met Thr Pro Lys Asp Thr Ser Leu Ala Leu Ala Met Val 180 185 190 Ser Phe Ile Leu Tyr Phe Asn Trp Asn Trp Val Gly Leu Val Leu Ser 195 200

Asp Asn Asp Glu Gly Asn Gln Phe Leu Thr Glu Leu Lys Lys Glu Thr His Asn Thr Glu Ile Cys Phe Ala Phe Val Asn Met Met Ala Ile Asn Glu Asn Ser Ser Met Lys Lys Thr Asp Met Tyr Tyr Asn Gln Ile Val Met Ser Thr Ala Asn Val Ile Ile Ile Tyr Gly Glu Arg Pro Ser Ile Ile Glu Leu Cys Phe Arg Thr Trp Thr Ser Pro Val Ile Gln Arg Ile Trp Val Thr Lys Ser Glu Leu Tyr Phe Pro Thr Ser Lys Arg Asp Leu Ser His Gly Thr Phe Tyr Gly Thr Leu Ala Phe Gln Gln His His Asp Val Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Trp Tyr His Leu Lys Ser Met Asp Leu Tyr Leu Leu Lys Pro Glu Trp Gly Phe Phe Glu Tyr Glu Thr Ser Ala Ser Tyr Cys Lys Ile Leu Met Ser Asn Ser Ser Asn Val Ser Leu Glu Trp Leu Met Glu Gln Lys Phe Asp Ile Ala Phe Asn Asp Asn Ser His Ser Ile Tyr Asn Ala Val Tyr Ala Met Ala His Ala Leu His Glu Lys Asn Leu Lys Gln Ile Asp Asn Gln Glu Ile Ser Tyr Gly Lys Gly Ala Ser Thr His Cys Leu Lys Leu His Ser Phe Leu Arg Thr Ile His Phe Thr Asn Pro Phe Gly Glu Arg Val Ile Met Lys Glu Arg Val Arg Val Gln Glu Asp Tyr Asp Ile Val His Leu Gln Asn Cys Ser Gln His Leu Arg Ile Lys Val Lys Ile Gly Gln Phe Ser Pro Tyr Phe Pro His Gly Gly Gln Phe His Leu Tyr Glu Asp Met Ile Asp Leu Ala Thr Gly Ser Arg Lys Met Pro Leu Ser Met Cys Ser Ala Asp Cys Arg Pro Gly Tyr Arg Lys Phe Trp Lys Glu Gly Met Ala Ala Cys Cys Phe Val Cys Ser Pro Cys Pro Asp Asn Glu Ile Ser Asn Glu Thr Thr Val Val Leu Trp Val Phe Val Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ile Leu Ser Tyr Ile Leu Ile Met Ser Leu Met Phe Cys Phe Leu Cys Ser Phe Phe Phe Ile Gly His Pro Asn Arg Gly Thr Cys Ile Leu Gln Gln Ile Thr Phe Gly Ile Val Phe Thr Val Ala Val Ser Thr Val Leu Ala Lys Thr Ile Thr Val Leu Leu Ala Phe Gln Val Thr Asp Thr Gly Arg Lys Leu Arg Asn Phe Leu Val Ser Gly Thr Pro Asn Tyr Ile Ile Pro Ile Cys Ser Leu Leu Gln Cys Thr Leu Cys Ala 645 "650 655 Ile Trp Leu Ala Val Ser Pro Pro Phe Val Asp Ile Asp Glu His Ser Glu His Gly His Ile Ile Ile Val Cys Asn Lys Gly Ser Val Met Ala Phe Tyr Cys Val Leu Gly Tyr Leu Ala Phe Leu Ala Leu Gly Ser Phe Thr Met Ala Phe Leu Ala Lys Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu Val Phe Cys Ser Val Trp Ile Thr.

				725					730					735	
Phe	Leu	Pro	Val 740	Tyr	His	Ser	Thr	Lys 745	Gly	Arg	Val	Met	Val 750	Ala	Val
Glu	Ile	Phe 755	Ser	Ile	Leu	Thr	Ser 760	Ser	Ala	Gly	Met	Leu 765	Gly	Сув	Val
Phe	Ala 770	Pro	Lys	Ile	Tyr	Ile 775	Ile	Leu	Met	Lys	Pro 780	Glu	Arg	Ile	Leu
Ser 785	Lys	Arg	Gln	Glu	Lys 790	Ser	Arg	Phe							
		(2)	INI	FORM	ATIO	1 FOI	R SE	Q ID	NO:	17:					

	(i)	SEQUENCE	CHARACTERISTICS:
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- (A) LENGTH: 3359 base pairs
 (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:

 - (A) NAME/KEY: Coding Sequence (B) LOCATION: 59...2452 (D) OTHER INFORMATION: GOVN13C

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

•	
CGGCACGAGC ACAGTCCACT CTGTCAGGGT TTAAGGCAGG AAAAACATGC TCATTTTG AT Met	60
GGT AAT ATT CTT CCT TCT CAA CAT TCC ATT TCT CCT GGC AAA TTT CAT Val Ile Phe Phe Leu Leu Asn Ile Pro Phe Leu Leu Ala Asn Phe Met 5 10 15	108
GGA TCC CAG ATG CTT TTG GAA AAT AAA TTT GAA TGA AAT CAA GGA TGA Asp Pro Arg Cys Phe Trp Lys Ile Asn Leu Asn Glu Ile Lys Asp Glu 20 25 30	156
AGT CCT TGG GAT GAC TTG TTC CTT CAT CCT TGA AAC AGT TCA GAA GAC Val Leu Gly Met Thr Cys Ser Phe Ile Leu Glu Thr Val Gln Lys Thr 35 40 45	204
TAT GGA CAA AGA TTA TTT CAA CCA GAC TCT GAA TGT CCT AAA TAC AAC Met Asp Lys Asp Tyr Phe Asn Gln Thr Leu Asn Val Leu Asn Thr Thr 50 55 60 65	252
TAC AAA CCA CAA ATA TGC CTT GGC ATT GGC CTT TAC AGT GGA TGA AAT Thr Asn His Lys Tyr Ala Leu Ala Leu Ala Phe Thr Val Asp Glu Ile 70 75 80	300
CAA CAG GAA TCC TGA TCT TTT ACC AAA TAT GTC TCT GAT TAT AAA ATA Asn Arg Asn Pro Asp Leu Leu Pro Asn Met Ser Leu Ile Ile Lys Tyr 85 90 95	348
CAA TTT GGG TCA TTG TGA TGG AAA AAC TGT AAC AAC TCT ATC CGA TTT Asn Leu Gly His Cys Asp Gly Lys Thr Val Thr Thr Leu Ser Asp Leu 100 105 110	396
ATT TAA TCC AAA TAA TCA TCT CCA TTT CCC CAA TTA TT	444
AGG GAT TAT GTG TTT GGT TCT GCT TAC AGG ACC ACA TTG GAG AGC ATC	492

Gly Ile Met Cys Leu Val Leu Leu Thr Gly Pro His Trp Arg Ala Ser 130 135 140 14	
TTT ATA TCT CTG GAT ATC CGT GTA TGT CTA CCT GTC TCC ACA TTT CCT Leu Tyr Leu Trp Ile Ser Val Tyr Val Tyr Leu Ser Pro His Phe Leu 150 155 160	540
TCA GCT TTC CTA TGG ACC TTT CTA CTC CAT CTT CAG TGA TAA TGA ACA Gln Leu Ser Tyr Gly Pro Phe Tyr Ser Ile Phe Ser Asp Asn Glu Gln 165 170 175	588
ATA TCC TTA TCT CTA TCA GAT GGG CCC AAA GGA CTC ATC ACT AGC ATT Tyr Pro Tyr Leu Tyr Gln Met Gly Pro Lys Asp Ser Ser Leu Ala Leu 180 185 190	636
GGC AAT GGT CTC CTT CAT AAT TTA CTT CAA GTG GAA CTG GGT TGG GCT Ala Met Val Ser Phe Ile Ile Tyr Phe Lys Trp Asn Trp Val Gly Leu 195 200 205	684
ATT TAT CTC AGA TGA TGA TCA AGG CAA TCA ATT TCT CTC AGA GTT GAA Phe Ile Ser Asp Asp Gln Gly Asn Gln Phe Leu Ser Glu Leu Lys 210 215 220 22	732
AAA AGA GAG CCA AAC CAA GGA TAT TTG CTT TGC CTT TGT GAA CAT GAT Lys Glu Ser Gln Thr Lys Asp Ile Cys Phe Ala Phe Val Asn Met Ile 5 230 235 240	780
ATC AGT CAG TGA TGT TTC ATA CTA TCA TAA AAC TGA AAT GTA CTA CAA Ser Val Ser Asp Val Ser Tyr Tyr His Lys Thr Glu Met Tyr Tyr Asn 245 250 255	828
CCA AAT TGT GAT GTC ATC CAC AAA GGT TAT TAT CAT TTA TGG GGA AAC Gln Ile Val Met Ser Ser Thr Lys Val Ile Ile Ile Tyr Gly Glu Thr 260 265 270	876
AAA CAG TAT TAT TGA ATT GAG CTT CAG AAT GTG GTC ATC TCC AGT TAA Asn Ser Ile Ile Glu Leu Ser Phe Arg Met Trp Ser Ser Pro Val Lys 275 280 285	924
ACA GAG AAT ATG GGT CAC CAC AAA ACA ATT TGA TTG CCC TAC CAG TAA Gln Arg Ile Trp Val Thr Thr Lys Gln Phe Asp Cys Pro Thr Ser Lys 290 295 300 30	972
GAG AGA CTT AAC TCA TGG CAC ATT CTA TGG GAC CCT TAC ATT TCT ACA Arg Asp Leu Thr His Gly Thr Phe Tyr Gly Thr Leu Thr Phe Leu His 310 315 320	1020
CCA CTA TGG TGA GAT TTC TGG CTT TAA AAA TTT TGT ACA GAC ACG GTA His Tyr Gly Glu Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Arg Tyr 325 330 335	1068
CAA TCT CAG AAG CAC AGA TTT ATA TCT AGT AAT GCC AGA GTG GAA ATA Asn Leu Arg Ser Thr Asp Leu Tyr Leu Val Met Pro Glu Trp Lys Tyr 340 345 350	1116
TTT TAA CTA TGA AGC CTC AGC ATC TAA CTG TAA AAT ACT GAG AAA CTA Phe Asn Tyr Glu Ala Ser Ala Ser Asn Cys Lys Ile Leu Arg Asn Tyr 355 360 365	1164
TTT ATC CAA TAT CTC ACT GGA ATG GCT AAT GGA ACA GAA ATT TGA CAT Leu Ser Asn Ile Ser Leu Glu Trp Leu Met Glu Gln Lys Phe Asp Met 370 375 380 38	1212
GTC ATT TAG TGA TTA TAG TCA CAA CAT ATA CAA TGC TGT ATA TGC CAT Ser Phe Ser Asp Tyr Ser His Asn Ile Tyr Asn Ala Val Tyr Ala Ile.	1260

5	390	395	400	
	CCA TGA GAA GAA T His Glu Lys Asn		TGA AAA TCA GGC . Glu Asn Gln Ala 415	1308
	GAA AGG AGA AAA T Lys Gly Glu Asn 425			1356
	GAC CCA CTT CAC T Thr His Phe Thr 440		Asn Arg Val Ile	1404
	AGA AGT AGT GCA T Glu Val Val His 455			1452
	ACA ACG CCT TGG G Gln Arg Leu Gly 470		GAT AGG ACA ATT : Ile Gly Gln Phe 480	1500
	TCC ACA GGG TCA F Pro Gln Gly Gln			1548
	TAC AGG AAG TAG A Thr Gly Ser Arg 505			1596
	TCC TGG ATT CAG A Pro Gly Phe Arg 520		Glu Glu Met Ala	1644
	TGT TTG CAA CCC (Val Cys Asn Pro 535		TGA AAT TTC TAA 1 Glu Ile Ser Asn 54	1692
	GGT ATT TTG GGT (Val Phe Trp Val 550		CCA TGA CAC TCC His Asp Thr Pro 560	1740
	_		ATT AAT CGT GTC 1 Leu Ile Val Ser 575	1788
	TTT TCT GTG CTC (Phe Leu Cys Ser 585		TGG CTA TCC TAA Gly Tyr Pro Asn 590	1836
	TAT CTT ACA GCA I Ile Leu Gln Gln 600		/ Ile Phe Phe Thr	1884
	CAC AGT TCT GGC (Thr Val Leu Ala 615		TGT GGT TCT GGC Val Val Leu Ala 62	1932
	AGA CCC AGG AAG A Asp Pro Gly Arg 630		CTT TTT GGT ATC Phe Leu Val Ser 640	1980
	-		ATT GCA ATG TAT 1 Leu Gln Cys Ile 655	2028

TCT GTG TGC AAT CTG GCT AGC AGT TTC TCC TCC CTT TGT TGA TAT TGA Leu Cys Ala Ile Trp Leu Ala Val Ser Pro Pro Phe Val Asp Ile Asp 660 665 670	2076
TGA ACA CTC TGA GCA TGG CCA CAT CAT CAT TGT GTG CAA CAA GGG CTC Glu His Ser Glu His Gly His Ile Ile Ile Val Cys Asn Lys Gly Ser 675 680 685	2124
CAT TAC TGC ATT CTA CTG TGT CCT GGG ATA CTT GGC CTG CCT GGC CTT Ile Thr Ala Phe Tyr Cys Val Leu Gly Tyr Leu Ala Cys Leu Ala Phe 690 695 700 70	2172
TGG AAG CTT CAC TAT AGC TTT CTT GGC AAA GAA CCT GCC TGA CAC ATT Gly Ser Phe Thr Ile Ala Phe Leu Ala Lys Asn Leu Pro Asp Thr Phe 710 715 720	2220
CAA CGA AGC CAA GTT CTT GAC CTT CAG CAT GCT AGT GTT CTG CGC TGT Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu Val Phe Cys Ala Val 725 730 735	2268
CTG GGT CAC CTT CCT CCC TGT CTA CCA TAG CAC CAA GGG CAA GGT CAT Trp Val Thr Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys Val Met 740 745 750	2316
GGT TGC TGT GGA GAT CTT CTC CAT CTT GGC ATC TAG TGC AGG GAT GCT Val Ala Val Glu Ile Phe Ser Ile Leu Ala Ser Ser Ala Gly Met Leu 755 760 765	2364
GGG ATG CAT CTT TGC ACC CAA AGT TTA CAT CAT TTT AAT GAG ACC AGA Gly Cys Ile Phe Ala Pro Lys Val Tyr Ile Ile Leu Met Arg Pro Asp 770 780 78	2412
CAG AAA TTC GAT CCA CAA AAT CAG GGA GAA ATC ATA TTT C TGAAAAGGTA Arg Asn Ser Ile His Lys Ile Arg Glu Lys Ser Tyr Phe 790 795	2462
TTTCAGGAAT TCTGTCAAAT GTAAAGTTGA TACATACACC CCAAATATTT AGTTACAGAG	2522
CATATATCTA GTTTTAGAAT CACTCTCACT GGTTCCTCTA GTTAAGCATA GAAGTACCAT	2582
ATGTACTGAT CTTGCATATG TTGTCTATAA AATCTTACAA TCATTCATTT GCTTAGTATC	2642
TTCTGGAAGA AGTAAAATTT TCAAATAACT AGTACAATTT TATTCATTAT TTTGCTTTCA	2702
TGAGGATTTC CCCCTGGTAA CTTCAAATAA ATTTTATAAG TCAGTTGAAT ATATAACCTT	2762
ACATAGAAAG TGAGTTCTAG GACAGACAGG GATTATACAT AGAAACAAAC TAACTAAAAA	2822
TCAACAAAGA TGAAATCAGA ACACATTTTC TTATTTCCAG TAGGAACACA TACTTGACAG	2882
AATACTGTCT TTTTTCAGC TGCTCTTTAA GATATTGGCC AATAGTCTAA GCTGAAAATG	2942
TTCTTTATCT ACTCTCAAAT ACAAAAATAT TATATCCAAC AATGGACAGA ATCTGAGAAC	3002
TCCTGTGGTT GAGTTAGGGA ATAGTTGGAA GATACTGAGA AGGAGGTGAC CCATAGGAAT	3062
ACAAAGCAGT CTCAACTAAC CTGGACAACC AAGGTCCCTC AGACACTGAG CCACTAACAA	3122
GTCAGCCTAC TCCAGCTGTT ATGAGGCCCC CAAAACATAT GCAACATAGG ATTGCCTGGT	3182
CCAGCCTCAG CAAGAGAATA CACACCTAAC CACAGAGAGA CTTCCCCAAG GGATTGGGGA	3242
GGTCTGGGGT TTGGAGAGTT GCGGATTGTC CCTTGATGAT TGGAAGGAGG TATTGGATGA	3302
GAATGAATCA GGGGGAAGAC TAGGAAGGGG ATAATGATGG AACTGTAAAA AAAAAAA	3359

- (2) INFORMATION FOR SEQ ID NO:48:
- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 798 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Met Val Ile Phe Phe Leu Leu Asn Ile Pro Phe Leu Leu Ala Asn Phe Met Asp Pro Arg Cys Phe Trp Lys Ile Asn Leu Asn Glu Ile Lys Asp Glu Val Leu Gly Met Thr Cys Ser Phe Ile Leu Glu Thr Val Gln Lys Thr Met Asp Lys Asp Tyr Phe Asn Gln Thr Leu Asn Val Leu Asn Thr Thr Thr Asn His Lys Tyr Ala Leu Ala Leu Ala Phe Thr Val Asp Glu Ile Asn Arg Asn Pro Asp Leu Leu Pro Asn Met Ser Leu Ile Ile Lys Tyr Asn Leu Gly His Cys Asp Gly Lys Thr Val Thr Thr Leu Ser Asp Leu Phe Asn Pro Asn Asn His Leu His Phe Pro Asn Tyr Leu Cys Asn Glu Gly Ile Met Cys Leu Val Leu Leu Thr Gly Pro His Trp Arg Ala Ser Leu Tyr Leu Trp Ile Ser Val Tyr Val Tyr Leu Ser Pro His Phe Leu Gln Leu Ser Tyr Gly Pro Phe Tyr Ser Ile Phe Ser Asp Asn Glu Gln Tyr Pro Tyr Leu Tyr Gln Met Gly Pro Lys Asp Ser Ser Leu Ala Leu Ala Met Val Ser Phe Ile Ile Tyr Phe Lys Trp Asn Trp Val Gly Leu Phe Ile Ser Asp Asp Asp Gln Gly Asn Gln Phe Leu Ser Glu Leu Lys Lys Glu Ser Gln Thr Lys Asp Ile Cys Phe Ala Phe Val Asn Met Ile Ser Val Ser Asp Val Ser Tyr Tyr His Lys Thr Glu Met Tyr Tyr Asn Gln Ile Val Met Ser Ser Thr Lys Val Ile Ile Ile Tyr Gly Glu Thr Asn Ser Ile Ile Glu Leu Ser Phe Arg Met Trp Ser Ser Pro Val Lys Gln Arg Ile Trp Val Thr Thr Lys Gln Phe Asp Cys Pro Thr Ser Lys Arg Asp Leu Thr His Gly Thr Phe Tyr Gly Thr Leu Thr Phe Leu His His Tyr Gly Glu Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Arg Tyr Asn Leu Arg Ser Thr Asp Leu Tyr Leu Val Met Pro Glu Trp Lys Tyr Phe Asn Tyr Glu Ala Ser Ala Ser Asn Cys Lys Ile Leu Arg Asn Tyr Leu Ser Asn Ile Ser Leu Glu Trp Leu Met Glu Gln Lys Phe Asp Met Ser Phe Ser Asp Tyr Ser His Asn Ile Tyr Asn Ala Val Tyr Ala Ile Ala His Ala Leu His Glu Lys Asn Leu Gln Glu Val Glu Asn Gln Ala Ile Asn Asn Ala Lys Gly Glu Asn Thr His Cys Leu Lys Leu Asn Ser Phe Leu Arg Lys Thr His Phe Thr Asn Ser Leu Gly Asn Arg Val Ile Met Lys Gln Arg Glu Val Val His Gly Asp Tyr Asn Ile Val His Met Trp Asn Phe Ser Gln Arg Leu Gly Ile Lys Val Lys Ile Gly Gln Phe Ser Pro His Phe Pro Gln Gly Gln Gln Leu His Leu Tyr Val Asp Met Thr Glu Leu Ala Thr Gly Ser Arg Lys Met Pro Ser Ser Val Cys Ser Ala Asp Cys His Pro Gly Phe Arg Arg Ile Trp Lys Glu Glu Met .

520 Ala Ala Cys Cys Phe Val Cys Asn Pro Cys Pro Glu Asn Glu Ile Ser 535 530 Asn Glu Thr Met Val Val Phe Trp Val Phe Val Lys His His Asp Thr 555 550 Pro Ile Val Lys Ala Asn Asn Arg Ile Leu Ser Tyr Leu Leu Ile Val 570 565 Ser Leu Met Phe Cys Phe Leu Cys Ser Phe Phe Phe Ile Gly Tyr Pro 590 585 580 Asn Arg Ala Thr Cys Ile Leu Gln Gln Ile Thr Phe Gly Ile Phe Phe 600 605 595 Thr Val Ala Ile Ser Thr Val Leu Ala Lys Thr Ile Thr Val Val Leu 615 620 Ala Phe Lys Val Thr Asp Pro Gly Arg Gln Leu Arg Ile Phe Leu Val 630 635 Ser Gly Thr Pro Asn Tyr Ile Ile Pro Ile Cys Ser Leu Leu Gln Cys 650 655 645 Ile Leu Cys Ala Ile Trp Leu Ala Val Ser Pro Pro Phe Val Asp Ile 665 670 Asp Glu His Ser Glu His Gly His Ile Ile Ile Val Cys Asn Lys Gly 685 Ser Ile Thr Ala Phe Tyr Cys Val Leu Gly Tyr Leu Ala Cys Leu Ala 695 700 Phe Gly Ser Phe Thr Ile Ala Phe Leu Ala Lys Asn Leu Pro Asp Thr 720 710 715 Phe Asn Glu Ala Lys Phe Leu Thr Phe Ser Met Leu Val Phe Cys Ala 730 725 Val Trp Val Thr Phe Leu Pro Val Tyr His Ser Thr Lys Gly Lys Val 745 750 740 Met Val Ala Val Glu Ile Phe Ser Ile Leu Ala Ser Ser Ala Gly Met 760 765 755 Leu Gly Cys Ile Phe Ala Pro Lys Val Tyr Ile Ile Leu Met Arg Pro 775 780 Asp Arg Asn Ser Ile His Lys Ile Arg Glu Lys Ser Tyr Phe 790

(2) INFORMATION FOR SEQ ID NO:49:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3012 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 3...2087
 - (D) OTHER INFORMATION: GOVN13B

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

AT GTC TAC CTG TCT CCA CAT TTC CTT CAG CTT TCC TAT GGA CCT TTC

Val Tyr Leu Ser Pro His Phe Leu Gln Leu Ser Tyr Gly Pro Phe

1 5 10 15

TAC TCC ATC TTC AGT GAT AAT GAA CAA TAT CCT TAT CTC TAT CAG ATG
Tyr Ser Ile Phe Ser Asp Asn Glu Gln Tyr Pro Tyr Leu Tyr Gln Met
20 25 30

GGC CCA AAG GAC TCA TCA CTA GCA TTG GCA ATG GTC TCC TTC ATA ATT

Gly Pro Lys Asp Ser Ser Leu Ala Leu Ala Met Val Ser Phe Ile Ile

35

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			TGG Trp													191
			TTT Phe													239
			GCC Ala													287
			ACT Thr													335
			ATC Ile 115													383
			TGG Trp													431
			GAT Asp													479
			ACC Thr													527
			TTT Phe													575
			ATG Met 195													623
			AAA Lys												GAA Glu	671
			GAA Glu													719
			AAT Asn													767
			GAA Glu												GAA Glu	815
			TGC Cys 275	Leu												863
			CTT Leu												GTG Val	911
CAT	· GGA	GAC	TAT	AAT	ATT	GTT	CAC	ATG	TGG	AAT	TTC	TCA	CAA	CGC	CTT	959

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His	Gly 305	Asp	Tyr	Asn	Ile	Val 310	His	Met	Trp	Asn	Phe 315	Ser	Gln	Arg	Leu	
				AAG Lys												1007
				TTA Leu 340												1055
				TCC Ser												1103
				AAG Lys												1151
				AAT Asn												1199
				GAA Glu												1247
				GTG Val 420												1295
				ATA Ile												1343
				GTG Val												1391
				AGC Ser											TTT Phe	1439
				TTC Phe						-						1487
				ACA Thr 500												1535
				ACA Thr												1583
				TTA Leu												1631
				TGT Cys												1679
				CCT Pro											CAT His	1727

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560 565 570 575	
GGC CAC ATC ATC ATT GTG TGC AAC AAG GGC TCC ATT ACT GCA TTC TAC Gly His Ile Ile Val Cys Asn Lys Gly Ser Ile Thr Ala Phe Tyr 580 585 590	1775
TGT GTC CTG GGA TAC TTG GCC TGC CTG GCC TTT GGA AGC TTC ACT ATA Cys Val Leu Gly Tyr Leu Ala Cys Leu Ala Phe Gly Ser Phe Thr Ile 595 600 605	1823
GCT TTC TTG GCA AAG AAC CTG CCT GAC ACA TTC AAC GAA GCC AAG TTC Ala Phe Leu Ala Lys Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe 610 615 620	1871
TTG ACC TTC AGC ATG CTA GTG TTC TGC GCT GTC TGG GTC ACC TTC CTC Leu Thr Phe Ser Met Leu Val Phe Cys Ala Val Trp Val Thr Phe Leu 625 630 635	1919
CCT GTC TAC CAT AGC ACC AAG GGC AAG GTC ATG GTT GCT GTG GAG ATC Pro Val Tyr His Ser Thr Lys Gly Lys Val Met Val Ala Val Glu Ile 640 655 655	1967
TTC TCC ATC TTG GCA TCT AGT GCA GGG ATG CTG GGA TGC ATC TTT GCA Phe Ser Ile Leu Ala Ser Ser Ala Gly Met Leu Gly Cys Ile Phe Ala 660 665 670	2015
CCC AAA GTT TAC ATC ATT TTA ATG AGA CCA GAC AGA AAT TCG ATC CAC Pro Lys Val Tyr Ile Ile Leu Met Arg Pro Asp Arg Asn Ser Ile His 675 680 685	2063
AAA ATC AGG GAG AAA TCA TAT TTC TGAAAAGGTA TTTCAGGAAT TCTGTCAAAT Lys Ile Arg Glu Lys Ser Tyr Phe 690 695	2117
GTAAAGTTGA TACATACACC CCAAATATTT AGTTACAGAG CATATATCTA GTTTTAGAA	T 2177
CACTCTCACT GGTTCCTCTA GTTATGCATA GAAGTACCAT ATGTACTGAT CTTGCATAT	G 2237
TTGTCTATAA AATCTTACAA TCATTCATTT GCTTAGTATC TTCTGGAAGA AGTAAAATT	
TCAAATAACT AGTACAATTT TATTCATTAT TTTGCTTTCA TGAGGATTTC CCCCTGGTA	
CTTCAAATAA ATTTTATAAG TCAGTTGAAT ATATAACCTT ACATAGAAAG TGAGTTCTA GACAGACAGG GATTATACAT AGAAACAAAC TAACTAAAAA TCAACAAAGA TGAAATCAG	
ACACATTTTC TTATTTCCAG TAGGAACACA TACTTGACAG AATACTGTCT TTTTTTCAG	
TGCTCTTTAA GATATTGGCC AATAGTCTAA GCTGAAAATG TTCTTTATCT ACTCTCAAA	
ACAAAAATAT TATATCCAAC AATGGACAGA ATCTGAGAAC TCCTGTGGTT GAGTTAGGG	
ATAGTTGGAA GATACTGAGA AGGAGGGTGA CCCATAGGAA TACAAAGCAG TCTCAACTA	
CCTGGACAAC CAAGGTCCCT CAGACACTGA GCCACTAACA AGTCAGCCTA CTCCAGCTG	
TATGAGGCCC CCAAAACATA TGCAACATAG GATTGCCTGG TCCAGCCTCA GCAAGAGAA	
ACACACCTAA CCACAGAGAG ACTTCCCCAA GGGATTGGGG AGGTCTGGGG TTTGGAGAG TGCGGATTGT CCCTTGATGA TTGGAAGGAG GTATTGGATG AGAATGAATC AGGGGGAAG	
CTAGGAAGGG GATAATGATG GAACTGTAAA AAAAATTAAA AAAAAAAAAA	3012

- (2) INFORMATION FOR SEQ ID NO:50:
- (i) SEQUENCE CHARACTERISTICS:

 - (A) LENGTH: 695 amino acids(B) TYPE: amino acid(C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MODECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Val Tyr Leu Ser Pro His Phe Leu Gln Leu Ser Tyr Gly Pro Phe Tyr 15 5

Ser Ile Phe Ser Asp Asn Glu Gln Tyr Pro Tyr Leu Tyr Gln Met Gly Pro Lys Asp Ser Ser Leu Ala Leu Ala Met Val Ser Phe Ile Ile Tyr Phe Lys Trp Asn Trp Val Gly Leu Phe Ile Ser Asp Asp Gln Gly Asn Gln Phe Leu Ser Glu Leu Lys Lys Glu Ser Gln Thr Lys Asp Ile Cys Phe Ala Phe Val Asn Met Ile Ser Val Ser Asp Val Ser Tyr Tyr His Lys Thr Glu Met Tyr Tyr Asn Gln Ile Val Met Ser Ser Thr Lys Val Ile Ile Ile Tyr Gly Glu Thr Asn Ser Ile Ile Glu Leu Ser Phe Arg Met Trp Ser Ser Pro Val Lys Gln Arg Ile Trp Val Thr Thr Lys Gln Phe Asp Cys Pro Thr Ser Lys Arg Asp Leu Thr His Gly Thr Phe Tyr Gly Thr Leu Thr Phe Leu His His Tyr Gly Glu Ile Ser Gly Phe Lys Asn Phe Val Gln Thr Arg Tyr Asn Leu Arg Ser Thr Asp Leu Tyr Leu Val Met Pro Glu Trp Lys Tyr Phe Asn Tyr Glu Ala Ser Ala Ser Asn Cys Lys Ile Leu Arg Asn Tyr Leu Ser Asn Ile Ser Leu Glu Trp Leu Met Glu Gln Lys Phe Asp Met Ser Phe Ser Asp Tyr Ser His Asn Ile Tyr Asn Ala Val Tyr Ala Ile Ala His Ala Leu His Glu Lys Asp Leu Gln Glu Phe Glu Asn Gln Ala Ile Asn Asn Ala Lys Gly Glu Asn Thr His Cys Leu Lys Leu Asn Ser Phe Leu Arg Lys Thr His Phe Thr Asn Ser Leu Gly Asn Arg Val Ile Met Lys Gln Arg Glu Val Val His Gly Asp Tyr Asn Ile Val His Met Trp Asn Phe Ser Gln Arg Leu Gly Ile Lys Val Lys Ile Gly Gln Phe Ser Pro His Phe Pro Gln Gly Gln Gln Leu His Leu Tyr Val Asp Met Thr Glu Leu Ala Thr Gly Ser Arg Lys Met Pro Ser Ser Val Cys Ser Ala Asp Cys His Pro Gly Phe Arg Arg Ile Trp Lys Glu Glu Met Ala Ala Cys Cys Phe Val Cys Asn Pro Cys Pro Glu Asn Glu Ile Ser Asn Glu Thr Asn Met Asp Gln Cys Ala Asn Cys Pro Glu Tyr Gln Tyr Ala Asn Thr Glu Lys Asn Lys Cys Ile Gln Lys Gly Val Ile Val Leu Ser Tyr Glu Asp Pro Leu Gly Met Ala Leu Ala Leu Ile Ala Phe Cys Phe Ser Ala Phe Thr Val Val Val Phe Trp Val Phe Val Lys His His Asp Thr Pro Ile Val Lys Ala Asn Asn Arg Ile Leu Ser Tyr Leu Leu Ile Val Ser Leu Met Phe Cys Phe Leu Cys Ser Phe Phe Phe Ile Gly Tyr Pro Asn Arg Ala Thr Cys Ile Leu Gln Gln Ile Thr Phe Gly Ile Phe Phe Thr Val Ala Ile Ser Thr Val Leu Ala Lys Thr Ile Thr Val Val Leu Ala Phe Lys Val Thr Asp Pro Gly Arg Gln Leu Arg Ile Phe Leu Val Ser Gly Thr Pro Asn Tyr Ile .

540 530 535 Ile Pro Ile Cys Ser Leu Leu Gln Cys Ile Leu Cys Ala Ile Trp Leu 550 555 Ala Val Ser Pro Pro Phe Val Asp Ile Asp Glu His Ser Glu His Gly 565 570 575 His Ile Ile Ile Val Cys Asn Lys Gly Ser Ile Thr Ala Phe Tyr Cys 580 585 590 Val Leu Gly Tyr Leu Ala Cys Leu Ala Phe Gly Ser Phe Thr Ile Ala 595 600 605 Phe Leu Ala Lys Asn Leu Pro Asp Thr Phe Asn Glu Ala Lys Phe Leu 615 620 Thr Phe Ser Met Leu Val Phe Cys Ala Val Trp Val Thr Phe Leu Pro 630 635 Val Tyr His Ser Thr Lys Gly Lys Val Met Val Ala Val Glu Ile Phe 645 650 Ser Ile Leu Ala Ser Ser Ala Gly Met Leu Gly Cys Ile Phe Ala Pro 665 660 670 Lys Val Tyr Ile Ile Leu Met Arg Pro Asp Arg Asn Ser Ile His Lys 675 680 Ile Arg Glu Lys Ser Tyr Phe 690

(2) INFORMATION FOR SEQ ID NO:51:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 435 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

CAGACTCTGA	GCTACACCCT	CCTTGTCTCC	CTCACACTCT	GCTTTCTCTC	TTCCTCGCTC	60
TTCATCGGCC	GCCCCAGCCC	TGCCACCTGC	CTCCTCTCAC	AGACCACCTT	TGCAGCTGTG	120
TTCACAGTGG	CTGTGTTTTT	CTGCAGGGCC	TTCCAGGCTA	TAAGGCCAGA	AAGCAGGATC	180
CGAAAGTGGA	TGGGTCCCCA	AAAAACAAAT	TCTGTTGTCT	TCCTTTGCTC	CTTTACCCAA	240
GTGACCCTCT	GTGGAATCTG	GCTGGGGACA	GAGCCTCCCT	TCGTAAACAA	GGACCCTCAG	300
TTCATGCCTG	GCTACATCAT	TATCCAGTGT	AATGAGGGCT	CCGTCACTGC	CTTCTACTCT	360
GTCTTGGGCT	ACTTGGGCTT	CTTGGTTTTA	GGGTCCCTTG	CTGTAGCCTT	TCTGGCAAGG	420
AACCTGCCTG	ATGCT					435

(2) INFORMATION FOR SEQ ID NO:52:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 145 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Gln Thr Leu Ser Tyr Thr Leu Leu Val Ser Leu Thr Leu Cys Phe Leu 1 10 Ser Ser Ser Leu Phe Ile Gly Arg Pro Ser Pro Ala Thr Cys Leu Leu 20 25 30 Ser Gln Thr Thr Phe Ala Ala Val Phe Thr Val Ala Val Phe Phe Cys 35 40 Arg Ala Phe Gln Ala Ile Arg Pro Glu Ser Arg Ile Arg Lys Trp Met 55 60 Gly Pro Gln Lys Thr Asn Ser Val Val Phe Leu Cys Ser Phe Thr Gln 70 75 80 . Val Thr Leu Cys Gly Ile Trp Leu Gly Thr Glu Pro Pro Phe Val Asn 85 Lys Asp Pro Gln Phe Met Pro Gly Tyr Ile Ile Ile Gln Cys Asn Glu 100 105 110 Gly Ser Val Thr Ala Phe Tyr Ser Val Leu Gly Tyr Leu Gly Phe Leu 125 120 115 Val Leu Gly Ser Leu Ala Val Ala Phe Leu Ala Arg Asn Leu Pro Asp 135 Ala 145

(2) INFORMATION FOR SEQ ID NO:53:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 474 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

CCCATTGTGA AGGCTAATAA CCAGACTCTG AGCTACACCC TCCTTGTCTC CCTCACACTC TGCTTTCTCT CTTCCTCGCT CTTCATCGGC CGCCCCAGCC CTGCCACCTG CCTCCTCTCA 120 CAGACCACCT TTGCAGCTGT GTTCACAGTG GCTGTGTTTT CTGCAGGGCC TTCCAGGCTA
TAAGGCCAGA AAGCAGGATC CGAAAGTGGA TGGGTCCCCA AAAAACAAAT TCTGTTGTCT 180 240 TCCTTTGCTC CTTTACCCAA GTGACCCTCT GTGGAATCTG GCTGGGGACA GAGCCTCCCT 300 TCGTAAACAA GGACCCTCAG TTCATGCCTG GCTACATCAT TATCCAGTGT AATGAGGGCT 360 CCGTCACTGC CTTCTACTCT GTCTTGGGCT ACTTGGGCTT CTTGGTTTTA GGGTCCCTTG 420 474 CTGTAGCCTT TCTGGCAAGG AACCCGCCAG ATACGTTCAA TGAGGCCAAG TTAA

(2) INFORMATION FOR SEQ ID NO:54:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 338 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

ACTCCCATTG	TGAAGGCCAA	CAACTGCCAG	CTCAGCTATC	TCCTGCTGTC	CTCCTTGGCC	60
CTCAGCTTCC	TCTGCCCCTT	CATGTTCATT	GGCCACCCAG	ACCCCATCAC	TTGTGCTGTG	120
CACNAGGCAG	ATTTTGGGGT	CACCTTCATG	GTCTGCACAT	CCACTGTGCT	GGCCAAGACC	180
ATCGTGGTGG	TGGCAGCCTT	CCATGCCACC	CAGGCAGACA	CTCAGCTTAG	GGGGTGGGCG	240
GGGACAGTCC	TCCTCAGCAC	CATCCTCACT	GTTCCCTGAC	CCAGGCAGCC	TTGTGTGCAC	300
TCTGGGTGAC	CAGATGGCCC	CCTCAGCCTG	TAAAATCT			338

(2) INFORMATION FOR SEQ ID NO:55:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 182 base pairs

 - (B) TYPE: nucleic acid(C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

AACCTNCCCG	ATACNTTCAA	TGAAGCCAAG	TTCTTGATGT	TCAGCATGCT	GATGTTATGT	60
ACTGTTTGAA	TTACCTTCCA	TACTGTGTAA	CATAGCACCA	AAGGGAAGGT	CATGGTTGCC	120
TTGGAAATAT	TCTCCACCTT	GACTTCCAGT	GCTGAGTGCT	AGGNTGTATC	TTCGCNCCAA	180

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AA . 182

- (2) INFORMATION FOR SEQ ID NO:56:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 37 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

ATTGGATCCA GGCCGCTCTG GACAAAATAT GAATTCT

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- (2) INFORMATION FOR SEQ ID NO:57:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 37 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

GGCACATGGA CGAAATCTTG GTACTCTTCA GAATTCT

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- (2) INFORMATION FOR SEQ ID NO:58:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 51 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

- (2) INFORMATION FOR SEQ ID NO:59:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1079 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Met Ala Ser Tyr Ser Cys Cys Leu Ala Leu Leu Ala Leu Ala Trp His 1 5 10 15 Ser Ser Ala Tyr Gly Pro Asp Gln Arg Ala Gln Lys Lys Gly Asp Ile.

Ile Leu Gly Gly Leu Phe Pro Ile His Phe Gly Val Ala Ala Lys Asp Gln Asp Leu Lys Ser Arg Pro Glu Ser Val Glu Cys Ile Arg Tyr Asn Phe Arg Gly Phe Arg Trp Leu Gln Ala Met Ile Phe Ala Ile Glu Glu Ile Asn Ser Ser Pro Ser Leu Leu Pro Asn Met Thr Leu Gly Tyr Arg Ile Phe Asp Thr Cys Asn Thr Val Ser Lys Ala Leu Glu Ala Thr Leu Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Ser Arg Leu Leu Ser Asn Lys Asn Gln Tyr Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln Gln Val Val Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile Thr Gly Arg Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Leu Ile Ala Met Pro Glu Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe Gly Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Gln Lys Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu Pro Val Asp Thr Phe Val Arg Ser His Glu Glu Gly Gly Asn Arg Leu Leu Asn Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn Ile Asn Ser Val Glu Thr Pro Tyr Met Asp Tyr Glu His Leu Arg Ile Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg

Asp Cys Gln Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Gly Glu Thr Asp Ala Ser Ala Cys Asp Lys Cys Pro Asp Asp Phe Trp Ser Asn Glu Asn His Thr Ser Cys Ile Ala Lys Glu Ile Glu Phe Leu Ala Trp Thr Glu Pro Phe Gly Ile Ala Leu Thr Leu Phe Ala Val Leu Gly Ile Phe Leu Thr Ala Phe Val Leu Gly Val Phe Ile Lys Phe Arg Asn Thr Pro Ile Val Lys Ala Thr Asn Arg Glu Leu Ser Tyr Leu Leu Phe Ser Leu Leu Cys Cys Phe Ser Ser Ser Leu Phe Phe Ile Gly Glu Pro Gln Asp Trp Thr Cys Arg Leu Arg Gln Pro Ala Phe Gly Ile Ser Phe Val Leu Cys Ile Ser Cys Ile Leu Val Lys Thr Asn Arg Val Leu Leu Val Phe Glu Ala Lys Ile Pro Thr Ser Phe His Arg Lys Trp Trp Gly Leu Asn Leu Gln Phe Leu Leu Val Phe Leu Cys Thr Phe Met Gln Ile Leu Ile Cys Ile Ile Trp Leu Tyr Thr Ala Pro Pro Ser Ser Tyr Arg Asn His Glu Leu Glu Asp Glu Ile Ile Phe Ile Thr Cys His Glu Gly Ser Leu Met Ala Leu Gly Ser Leu Ile Gly Tyr Thr Cys Leu Leu Ala Ala Ile Cys Phe Phe Phe Ala Phe Lys Ser Arg Lys Leu Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Thr Phe Ser Met Leu Ile Phe Phe Ile Val Trp Ile Ser Phe Ile Pro Ala Tyr Ala Ser Thr Tyr Gly Lys Phe Val Ser Ala Val Glu Val Ile Ala Ile Leu Ala Ala Ser Phe Gly Leu Leu Ala Cys Ile Phe Phe Asn Lys Val Tyr Ile Ile Leu Phe Lys Pro Ser Arg Asn Thr Ile Glu Glu Val Arg Ser Ser Thr Ala Ala His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg Pro Asn Ile Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly Ser Ile Pro Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Arg Phe Pro Gln Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ser Leu Thr Gln Gln Gln Gln Gln Gln Pro Leu Thr Leu His Pro Gln Gln Gln Gln Pro Gln Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met Ala His Arg Asn Ser Met Arg Gln Asn Ser Leu Glu Ala Gln Arg Ser Asn Asp Thr Leu Gly Arg His Gln Ala Leu Leu Pro Leu Gln Cys Ala Asp Ala Asp Ser Glu Met Thr Ile Gln Glu Thr Gly Leu Gln Gly Pro Met Val Gly Asp His Gln Pro Glu Met Glu Ser Ser Asp Glu Met Ser Pro Ala Leu Val Met Ser Thr Ser Arg Ser Phe Val Ile Ser Gly Gly Gly Ser Ser Val .

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1065 1070 1060 Thr Glu Asn Val Leu His Ser 1075

- (2) INFORMATION FOR SEQ ID NO:60:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 3...3
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 12...12
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 15...15
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base

 - (B) LOCATION: 18...18
 (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

BTNYAYCARR TNGCNMCNAA RGAYAC

- (2) INFORMATION FOR SEQ ID NO:61:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 6...6
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 9...9
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 12...12
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 18...18

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(D) OTHER INFORMATION: Inosine	
(A) NAME/KEY: Modified Base (B) LOCATION: 2121	
(D) OTHER INFORMATION: Inosine	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:	
GYRTKNGCNR YNRCRTRNAC NRCRTT	26
(2) INFORMATION FOR SEQ ID NO:62:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	·
(ix) FEATURE:	
(A) NAME/KEY: Modified Base (B) LOCATION: 33	
(D) OTHER INFORMATION: Inosine	
(A) NAME/KEY: Modified Base (B) LOCATION: 99	
(D) OTHER INFORMATION: Inosine	
(A) NAME/KEY: Modified Base (B) LOCATION: 1212	
(D) OTHER INFORMATION: Inosine	
(A) NAME/KEY: Modified Base (B) LOCATION: 1313	
(D) OTHER INFORMATION: Inosine	
(A) NAME/KEY: Modified Base	
(B) LOCATION: 2424 (D) OTHER INFORMATION: Inosine	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:	
MRNTGYCCNK ANNAYMARTA YGCNAA	26
(2) INFORMATION FOR SEQ ID NO:63:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 base pairs	
(B) TYPE: nucleic acid	
<pre>(C) STRANDEDNESS: single (D) TOPOLOGY: linear</pre>	

(ix) FEATURE:

- (A) NAME/KEY: Modified Base(B) LOCATION: 2...2(D) OTHER INFORMATION: Inosine

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(A) NAME/KEY: Modified Base

- (B) LOCATION: 5...5
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 8...8
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 11...11
 (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base(B) LOCATION: 14...14
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 20...20
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 26...26
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 29...29
- (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

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GNCKNAYNAR NATNAYRTAN MWYTTNGGNA C

(2) INFORMATION FOR SEQ ID NO:64:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: Modified Base
- (B) LOCATION: 3...3
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 6...6
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 9...9
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
 (B) LOCATION: 12...12

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- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 16...16
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 24...24
- (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

ATNWSNYTNR TNTTYNGYTT YYTNTG

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- (2) INFORMATION FOR SEQ ID NO:65:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 2...2
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 5...5
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 11...11
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 17...17
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 20...20
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 23...23
 - (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

RNATNSWRAA NAYYTCNACN RCNACCAT

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- (2) INFORMATION FOR SEQ ID NO:66:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs

- (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ix) FEATURE: (A) NAME/KEY: Modified Base
- - (B) LOCATION: 6...6
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 9...9
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base (B) LOCATION: 12...12

 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 15...15
 - (D) OTHER INFORMATION: Inosine
 - (A) NAME/KEY: Modified Base
 - (B) LOCATION: 21...21
 - (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

GAYACNCCNA TNGTNAARGC NAAYAA

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- (2) INFORMATION FOR SEQ ID NO:67:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: Modified Base
- (B) LOCATION: 3...3
 (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 6...6
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 12...12
- (D) OTHER INFORMATION: Inosine
- (A) NAME/KEY: Modified Base
- (B) LOCATION: 15...15
- (D) OTHER INFORMATION: Inosine

- (A) NAME/KEY: Modified Base
- (B) LOCATION: 24...24
- (D) OTHER INFORMATION: Inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

AANGTNAYCC ANACNSWRCA RAANAC

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- (2) INFORMATION FOR SEQ ID NO:68:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2550 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

ATGAAGCAGC TCTGCGCTTT CACTATTTCT TTGTTGTTTC TGAAGTTTTC TCTCATCCTG TGCTGTTTGA CTGAACCAAG TTGCTTTTGG AGAATAAGGA ATAGTGAAGA TAGTGATGGA GATTTACAAA GGGAATGTCA TTTTTACCTT TGGAAAACTG ATGAACCTAT TGAAGATAGT 180 TTTTATAATT ATGATTTAAG TTTTAGAATT GCAGCAAGTG AATATGAGTT TCTTCTCGTA ATGTTTTTTG CTATCGATGA GATCAACAGG AATCCTTATC TTTTACCCAA CATAACTTTG 240 300 ATGTTCTCCT TCATTGGTGG AAACTGTCAG GATTTATTGA GAGTTATGGA CCAAGCATAT 360 ACACAAATAA ATGGACATAT GAATTTTGTT AATTATTTCT GTTATTTAGA TGATTCATGT 420 GCCATAGGTC TTACAGGACC ATCATGGAAA ACTTCCTTAA AACTGGCAAT GCACTCTTCG 480 ATGCCACTGG TTTTCTTTGG ACCATTTAAT CCTAACCTAC GCGACCATGA CCGGCTGCCC 540 CATGTCCATC AGGTAGCCCC CAAGGACACA CATTTGTCCC ATGGCATGGT CTCCTTGATG 600 TTTCACTTTA GATGGACTTG GATAGGACTG GTCATCTCAG ATGATGACCA GGGTATTCAG TTTCTCTCAG ATTTAAGAGA AGAAAGCCAA AGGCATGGGA TCTGTTTAGC TTTTGTTAAT 720 ATGATCCCAG AAAACATGCA GATATACATG ACAAGGGCTA CAATATATGA TAAACACATT 780 ATGACATCTT CAGCAAAGGT TGTTATCATT TATGGTGAAA TGAACTCTAC TCTAGAAGCA 840 AGCTTTAGAA GATGGGAAGA GTTAGGTGCT CGGAGAATCT GGATCACAAC CTCACAATGG GATGTCATCA CAAATAAAAA AGACTTCACC CTTAATCTCT TCCATGGGAT CATCACTTTT 960 GAACATCATA GATTTGAGAT TCCTAAATTA AATAATTCA TGCAAACAAT GAACACTGCC AAATACCCAG TAGATATTTC TCATACTATA TTGGAGTGGA ATTATTTTAA TTGTTCAATA 1020 1080 TCTAAGAACA GCATTAGAAT GCATCATATT ACATTCAACA ACACCTTGGA ATGGACATCA CTGCACAACT ATGATGTGGC GATGAGTGAT GAAGGTTACA ATTTGTACAA TGCTGTTTAT 1200 GCTGTGGCCC ACACCTACCA TGAATACATT TTTCAACAAG TAGAGTCTCA GAAAAAGGCA AAACCCAAAA GATATTTCAC TGCTTGTCAG CAGGTGTCTT CCTTGATGAA AACCAGGGTA 1260 1320 TTTACGAACC CTGTTGGAGA ACTGGTGAAC ATGAAGCATA GGGAAAATCA GTGTACAGAG TATGATATTT TCATCATTTG GAATTTTCCA CAAGGCCTTG GATTAAAAGT GAAAATAGGA AGCTATTTAC CTTGTTTTCC ACAGAGACAA AAACTTCATA TATCTGATGA TTTGGAATGG 1500 GCCAAGGGAG GAACATCACC TCAGGTTCCC TCCTCCGTGT GTAGTGTGGC ATGTACTGCT GGATTCAGGA AAATTTATCA AAAAGAAACA GCAGACTGCT GCTTTGATTG TGTTCAGTGC 1620 CCAGAAAATG AGATTTCCAA CGAAACAGAT ATGGAACAGT GTGTGAGGTG TCCAGATGAT AAGTATGCCA ACATAGAGCA AACCCACTGC CTCTCAAGAG CTGTATCATT TCTGGCTTAT GAAGATTCAT TGGGGATGGC TCTAGGCTGC ATGGCACTGT CCTTCTCAGC CATCACAATT CTAATCCTCG TCACATTTGT GAAGTACAAA GATACTCCCA CTGTGAAGGC CAATAACCGC 1860 ATTCTCAGCT ACATCCTGCT CATCTCTCTC GTCTTCTGCT TTCTCTGCTC CCTGCTCTTC 1920 ATTGGACCTC CCGACCAGGT CACCTGCATC TTTCAGCAGA CCACATTTGG AGTATTGTTC 1980 ACTGTGTCTG TTTCTACAGT GTTGGCCAAA ACAATAACTG TGGTCATGGC TTTCAAGCTC ACTACTCCAG GAAGAAGGAT GAGAGGGATG ATGATGACAG GGGCACCTAA GTTGGTCATT 2040 CCCATTTGTA CCCTGATCCA ACTTGTTCTC TGTGGAATCT GGTTGGTCAC ATCTCCTCCC 2160 TTTATTGACA GAGACATACA ATCTGAGCAT GGGAAGATTG TCATTCTTTG CAATAAAGGC TCAGTCATTG CCTTCCACGT CGTCCTGGGA TACTTGGGCT CCTTGGCTCT GGGGAGCTTC 2280 ACGTTGGCTT TCCTGGCTAG GAACCTTCCT GACACATTCA ATGAAGCCAA GTTCCTAACT TTCAGCATGC TGGTGTTCTG CAGTGTCTGG ATCACCTTCC TCCCTGTCTA CCACAGCACC 2400 AGGGGGAGGG TCATGGTGGT TGTGGAGGTT TTCTCCATCT TGGCTTCTAG TGCAGGGTTG 2460 CTAATGTGTA TCTTTGTCCC AAAGTGTTAT GTTATTTTAA TTAGACCAGA TTCAAATTTT 2520 ATAAAGAACC ACAAAGGTAA ATTGCTTTAT 2550

(2) INFORMATION FOR SEQ ID NO:69:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2424 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

ATGAAGCAGC	TCTGCACTTT	CACTATTTCA	TTGTTGTTTC	TGAAGTTTTC	TCTCATCTTG	60
TGCTGTTGGA	GTGAACCAAG	CTGCTTTTGG	AGGATAAAGA	AGAGTGAAGA	TAATGATGGA	120
GATTTACAAA	GGGAGTGTCA	TTTTTACCTT	TGGAAAACTG	ATGAACCTAT	TGAAGATAGT	180
TTTTATAATT	ATGATTTAAG	TTTTAGAATT	GCAGGAAGTG	AATATGAGCT	TCTTCTGGTA	240
ATGTTTTTTG	CTACTGATGA	GATCAACAAG	AATCCTTATC	TTTTACCCAA	CATGAGTTTG	300
ATGTTCTCCA	TCATTGGTGG	AAACTGTCAT	GATTTATTGA	GAAGTCTGGA	TCAAGAATAT	360
GCACAAATAG	ATGGACATAT	GAATTTTGTT	AATTATTTCT	GTTATTTAGA	TGATTCATGT	420
GCCACAGGCC	TTACAGGACC	ATCATGGAAA	ACATCCTTAA	AACTGGCAAT	GCATTCTTCA	480
ATGCCACTGG	TTTTCTTTGG	ACCATTTAAT	CCTAACCTAC	GCGACCATGA	CCGGCTGCCC	540
CATGTCCATC	AGGTAGCCCC	CAAGGACACA	CATTTGTCCC	ATGGCATGGT	CTCCTTGATG	600
TTTCATTTTA	GGTGGACTTG	GATAGGACTG	GTCATCTCAG	ATGATGATCA	GGGTATTCAG	660
TTTCTCTCAG	ATTTAAGAGA	AGAAAGCCAA	AGGCATGGGA	TCTGTTTGGC	TTTTGTTAAT	720
ATGATCCCAG	AAAACATGCA	GATATACATG	ACAAGGGCTA	CAATATATGA	TACACAAATT	780
ATGACATCTT	CAGCAAAGGT	TGTTATCATT	TATGGTGACA	TGAACTCTAC	TCTAGAAGCA	840
AGCTTTAGAA	GATGGGAAGA	GTTAGGTGCT	CGGAGAATCT	GGATCACAAC	CACACAATGG	900
GATGTCATCA	CAAATAAAAA	AGACTTCACC	CTTAATCTCT	TCCATGGGAC	TATTACTTTT	960
GCACACCACA	AAGATGAGAT	TCCTAAATTT	AGGAATTTTA	TGCAAACAAA	GAAAACTGCC	1020
AAATACCTTG	TAGATATTTC	TCATACTATT	TTGGAGTGGA	ATTATTTTAA	TTGTTCAATC	1080
TCTAAGAACA	GCAGTAAAAT	GGGTCATTTT	ACATTCAACA	ACACATTGCA	ATGGACAGCA	1140
CTGCACAACT	ATGATATGGC	CCTGAGCGAT	GAAGGTTACA	ATTTGTATAA	TGCTGTTTAT	1200
GCTGTGGCCC	ACACCTACCA	TGAATACATT	CTTCAACAAG	TAGAGTCTÇA	GAAAAAGGCA	1260
AAACCCAAAA	GATATTTCAC	TGCTTGTCAG	CAGGTGTCTT	CCTTGATGAA	AACCAGGGTA	1320
TTTATGAACC	CTGTTGGAGA	ACTGGTGAAC	ATGAAGCATA	GGGAAAATCA	GTGTACAGAG	1380
TATGATATTT	TCATCATTTG	GAATTTTCCA	CAAGGCCTTG	GATTAAAAGT	GAAAGTAGGA	1440
AGCTATTTAC	CTTGCTTTCC	AAAGAGTCAA	CAACTTCATA	TAGCTGATGA	TTTGGAATGG	1500
GCCATGGGAG	GAACATCAGT	GGATATGGAA	CAGTGTGTGA	GATGTCCAGA	TATAAATAT	1560
GCCAATTTAG	AGCAAACCCA	CTGCCTCCAA	AGAACGGTGT	CATTTCTGGC	TTATGAAGAT	1620
CCATTGGGGA	TGGCTCTAGG	CTGCATGGCA	CTGTCCTTCT	CGGCCATCAC	AATTCTAGTC	1680
CTCGTCACAT	TTGTGAAGTA	CAAGGATACT	CCCATTGTGA	AGGCCAATAA	CCGCATTCTC	1740
AGCTACATCC	TGCTCATCTC	TCTCGTCTTC				1800
CATCCCGACC	AGGTCACCTG	CATCTTGCAG	CAGACCACAT	TTGGAGTATT	GTTCACTGTG	1860
		CAAAACAATA				1920
		GATGATGATG				1980
TGTACCCTGA	TCCAACTTGT	TCTCTGTGGA	ATCTGGTTGG	TCACATCTCC	TCCCTTTATT	2040
		ACATGGGAAG				2100
GTTGCCTTCC	ACGTCGTCCT	GGGATACTTG				2160
GCTTTCTTGG	CTAGGAACCT			CCAAGTTCCT		2220
ATGCTGGTGT	TCTGCAGTGT	CTGGATCACC	TTCCTCCCTG	TCTACCACAG	CACCAGGGGG	2280
AAGGTCATGG	TGGTTGTGGA	GGTTTTCTCC	ATCTTGGCTT	CTAGTGCAGG	GTTGCTAATG	2340
TGTATCTTTG		TTATGTTATT	TTAATTAGAC	CAGATTCAAA	TTTTATACAG	2400
AACCACAAAG	GTAAATTGCT	TTAT				2424

- (2) INFORMATION FOR SEQ ID NO:70:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2409 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

		TGATAAACCA			TTCACTTTTA	60
AAGTTTAGAA	TTGCAGCAAG	TGAATATGAG	TTTCTTCTGG	TAATGTTTTT	TGCTACTGAT	120
GAGATCAACA	AGAATCCTTA	TCTTTTACCC	AACATAACTT	TGATGTTCTC	CATCATTGGT	180
GGAAACTGTC	ATGATTTATT	GAGAGGTTTG	GATCAAGCAT	ATACACAAAT	AAATGGACAT	240
ATGAATTTTG	TTAATTATTT	CTGTTATTTA	GATGATTCAT	GTGCCATAGG	TCTTACAGGA	300
CCATCATGGA	AAACATCCTT	AAATCTGGCA	ATGCATTCTT	CAATGCCACT	GGTTTTCTTT	360
GGATCATTTA	ATCCTAACCT	ACATGACCAT	GACCGGCTGC	ACCATGTCCA	TCAAGTAGCC	420
ACCAAGGACA	CACATTTGTC	CCATGGCATT	GTCTCCTTGA	TGTTTCATTT	TAGATGGACT	480
TGGATAGGAC	TGGTCATCTC	AGATGATGAC	AAGGGTATTC	AGTTTCTCTC	AGATTTAAGA	540
GAAGAAAGCC	AAAGGCATGG	GATCTGTTTA	GCTTTTGTTA	ATATGATCCC	AGAAAACATG	600
CAGATATACA	TGACAAGGGC	TACAATATAT	GATAAACAAA	TTATGACGTC	TTTAGCAAAA	660
GTTGTTATCA	TTTATGGTGA	AATGAACTCT	ACACTAGAAG	TAAGCTTTAG	AAGATGGGAA	720
AATTTAGGTG	CTCGGAGAAT	CTGGATCACA	ACCTCACAAT	GGGATGTCAT	CACAAATAAA	780
AAAGAATTCA	CCCTTAATCT	CTTCCATGGG	ACTATTACTT	TTGCACACCG	CAGATTTGAG	840
ATTCCTAAAT	TTAAAAAATT	TATGCAAACA	ATGAACACTG	CCAAATACCC	AGTAGATATT	900
TCTCATACTA	TATTGGAGTG	GAATTATTTT	AATTGTTCAA	TCTCTAAGAA	CAGCAGTAAA	960
ATGGATCATA	TTACATTCAA	CAACACATTG	GAATGGACAG	CACTGCACAA	CTATGATATG	1020
GTGATGAGTG	ATGAAGGTTA	CAATTTGTAT	AATGCTGTTT	ATGCTGTGGC	CCACACCTAC	1080
CATGAACATA	TTTTTCAACA	AGTAGAGTCT	CAGAAAAAGG	CAAAACCCAA	AAGATTTTTC	1140
ACTGTTTGTC	AGCAGGTGTC	TTCCTTGATG	AAAACCAGGG	TATTTACTAA	CCCTGTTGGA	1200
GAACTGGTGA	ACATGAAGCA	TAGGGAAAAT	CAGTGTACAG	AGTATGACAT	TTTCCTCATT	1260
TGGAACTTTC	CACAAGGCCT	TGGATTAAAA	GTGAAAATAG	GAAGCTATTT	ACCTTGTTTT	1320
CCACAGAGAC	AAGAACTTCA	TATATCTGAT	GATTTGGAAT	GGGCCATGGG	AGGAACATCA	1380
GTGGTTCCCT	CCTCTGTGTG	TAGTGTGGCA	TGTACTGCAG	GATTCAGGAA	AATTCATCAG	1440
AAAGAAACAG	CAGACTGCTG	CTTTGATTGT	GTTCAGTGCC	CAGAAAATGA	GGTTTCCAAT	1500
GAAACAGATA	TGGAACAGTG	TGTGAAGTGT	CCATATGATA	AGTATGCCAA	CATAGAGAAA	1560
ACCCACTGCC	TCTCAAGAGC	TGTATCATTT	CTGGCTTATG	AAGATCCATT	GGGGATAGCT	1620
CTAGGCTGCA	TAGCACTGTC	CTTCTCAGCC	ATCACAATTC	TAGTACTAAT	CACATTTTTG	1680
AAGTACAAGG	ATACTCCCAT	TGTGAAGGCC	AATAACCGCA	TTCTCAGCTA	CATCCTGCTC	1740
ATCTCTCTAG	TCTTCTGCTT	TCTCTGCTCC	CTGCTCTTCA	TTGGACATCC	AAACCAGGTC	1800
TCCTGCGTCT	TGCAGCAGAC	CACATTTGGA	GTATTTTTCA	CTGTGTCTGT	TTCTACAGTG	1860
TTGGCCAAAA	CAATAACTGT	GGTCATGGCT	TTCAAGCTCA	CTACTCCAGG	AAGAAGAATG	1920
AGAGAGATGT	TGGTAACAGG	GGCACCTAAG	TTGGTCATTC	CCATTTGTAC	CCTAATCCAA	1980
TTTGTTCTCT	GTGGAATCTG	GTTGATAACA	TCTCCTCCAT	TTATTGACAG	AGATATACAA	2040
TCTGAGCATG	GGAAGATTGT	CATTCTTTGC	AATAAAGGCT	CTGTCATTGC	CTTCCATGTT	2100
GTCCTGGGAT	ACTTGGGCTC	CTTGGCTCTG	GGGAGCTTCA	CTTTGGCTTT	CTTGGCTAGG	2160
AACCTTCCTG	ACACATTCAA	TGAAGCCAAA	TTCCTGACTT	TCAGCATGCT	GGTGTTCTGC	2220
AGTGTCTGGA	TCACCTTTCT	CCCTGTCTAC	CATAGCACCA	GGGGGAAGGT	CATGGTGGTT	2280
GTGGAGGTTT	TCTCAATCTT	GGCTTCTAGT	GCAGGGTTGC	TAATGTGTAT	CTTTGTCCCA	2340
AAGTGTTATG	TTATTTTAGT	TAGACCAGAT	TCAAATTTTA	TACGGAAGTA	CAAAGATAAA	2400
TTTCGTTAT				•		2409

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2556 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

ATGTTCATTT	TCATGGGAGT	CTTCTTCCTA	CTTAATATTA	CACTTCTCAT	GGCCAATTTC	60
ATTGATCCCA	GGTGCTTTTG	GAGAATAAAT	TTGGATGAAA	TAACGGATGA	ATATTTGGGA	120
TTATCTTGTG	CTTTCATCCT	GGCAGCTGTT	CAGACACCCA	TTGAAAAAGA	TTATTTCAAC	180
ACGACTCTTA	ATTTTCTAAA	AACTACTAAA	AACCACAAAT	ATGCTTTGGC	ATTGGTGTTT	240
GCAATGGATG	AAATCAACAG	ATATCCTGAT	CTTTTACCAA	ATATGTCTTT	GATTATCAGA	300
TACTCTTTGG	GCCATTGTGA	TGGAAAAACT	GTAACACCTA	CACCATATTT	ATTTCATAGA	360
AAAAAGCAAA	GCCCTATTCC	TAATTATTTC	TGTAATGAAG	AGAGTATGTG	TTCATTTCTG	420
CTTTCAGGAC	CCAATTGGGA	TGAATCTTTA	AGTTTCTGGA	AGTACCTGGA	CAGCTTCTTA	480
TCTCCACGTA	TCCTTCAGCT	TTCCTATGGA	TCTTTCAGTT	CCATCTTCAG	TGATGATGAA	540
CAATATCCCT	ATCTCTATCA	GATGGCCCCA	AAAGACACAT	CTCTAGCATT	GGCAATGGTC	600
TCCTTCATAC	TTTATTTGAA	ATGGAATTGG	ATTGGCCTTG	TCATCCCAGA	TGATGATCAA	660

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GGAAACCAAT	TTCTTTTAGA	GTTGAAGAAA	CAGAGTGAAA	ACAAAGAAAT	TTGCTTTGCC	720
TTTGTGAAAA	TGATCTCTGT	TGATGAAGTT	TCATTTCCAC	AAAAAACTGA	AATAAACTAC	780
AAACAAATTG	TGAAGTCACT	AACAAATGTT	ATTATCATTT	ATGGAGAAAC	ATATAATITC	840
ATTGATTTGA	TCTTCAGAAT	GTGGGAACCT	CCCATTTTAC	AGAGAATATG	GATCACCACA	900
AAACAATTGA	ATTTCCCTAC	CAGTAAGACA	GACATAAGTC	ATGACACATT	CTATGGATCA	960
CTTACTTTTC	TACCCCACCA	TGGTGAGATT	TCTGGCTTTA	AAAATTTTGT	ACAGACATGG	1020
TTCCATCTCA	GAAACACAGA	TTTATGTCTA	GTAATGCCAG	AGTGGAAATA	TATTAACTCT	1080
GAAGACTCAG	CATCTAATTG	TAAAATACTT	AAGAACAGTT	CATCTGATGC	CTCATTTGAT	1140
TGGCTAATGG	AAGAGAAGCT	TGACATGGCC	TTTAGTGAGA	ATAGTCATAA	CATATATAAT	1200
GCTGTGCATG	CCATAGCCCA	TGCCCTCCAT	GAGATGAATC	TGCAACAGGC	TGATAATCAG	1260
GCAATAGATA	ATGGAAAAGG	AGCCAGTTCT	CACTGCTTGA	AGGTAAACTC	CTTTCTAAGA	1320
AGGACCTACT	TCACTAATCC	TCTTGGGGAC	AAAGTGTTTA	TGAAGCAAAG	AGTAATAATG	1380
CAGGATGAAT	ATGACATTGT	TCACTTTGCG	AATCTCTCAC	AACACCTTGG	GATTAAGATG	1440
AAGTTAGGAA	AGTTCAGCCC	ATATTTACCA	CATGGTCGAC	ACTCTCACTT	ATACGTAGAC	1500
ATGATTGAGT	TGGCCACAGG	AAGAAGAAAG	ATGCCATCCT	CTGTGTGCAG	TGCAGATTGT	1560
AGTCCTGGAT	TCAGAAGATT	ATGGAAGGAG	GGAATGGCAG	CCTGCTGTTT	TGTTTGCAGC	1620
CCCTGCCCTG	AAAATGAAAT	TTCTAATGAG	ACAAATATGG	ATCAATGCGT	GAATTGTCCA	1680
GAATACCAAT	ATGCCAACAC	AGAACAGAAC	AAATGTATTC	AGAAAGGTGT	CACCTTCCTA	1740
AGCTATGAAG	ACCCCTTGGG	GATGGCACTT	GCCTTAATGG	CCTTCTGCTT	CTCTGCATTC	1800
ACAGCTGTGG	TACTTTGTGT	CTTTGTGAAG	CACCATGACA	CTCCTATTGT	GAAGGCCAAT	1860
AACAGAAGCC	TCAGCTATCT	ATTACTCATG	TCACTCATGT	TCTGTTTTCT	GTGCTCCTTT	1920
TTCTTCATTG	GCCTTCCAAA	CAAAGTCATC	TGTGTCTTAC	AGCAAATCAC	ATTTGGAATT	1980
GTATTCACTG	TGGCTGTTTC	CACAGTTCTG	GCCAAAACAG	TCACTGTGGT	TCTAGCTTTC	2040
AAAGTCACAG	TCCCAGGAAG	AAGATTGAGA	TACTTCCTTG	TATCAGGGAC	ACTAAACTAC	2100
ATTATTCCTA	TATGTTCCCT	ACTCCAATGT	GTTCTGTGTG	CAATCTGGCT	AGCAGTCTCT	2160
CCTCCCTTTG	TTGATATTGA	TGAACACTCT	CAGCATGGCC	ACATCATCAT	TGTGTGCAAC	2220
AAGGGCTCAG	TTACTGCATT	CTACTGTGTC	CTTGGATACT	TGGCCTGCCT	GGCACTGGGA	2280
AGCTTCACTT	TGGCTTTCTT	GGCCAAGAAT	CTGCCTGATG	CATTCAATGA	AGCCAAGTTC	2340
TTGACCTTCA	GCATGCTAGT	GTTCTGCAGT	GTCTGGGTCA	CCTTCCTCCC	TGTGTACCAT	2400
AGCACAAAGG	GCAAACACAT	GGTTGCTGTG	GAGATCTTCT	CTATCTTGGC	ATCCAGTGCA	2460
GGGATGCTTG	GATGTATTTT	TGTACCCAAG	ATTTATATCA	TTTTAATGAG	ACCAGAGAGA	2520
AATTCTACCC	AAAAGATCAG	AGAAAAATCA	TATTTT			2556

(2) INFORMATION FOR SEQ ID NO:72:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2169 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

ATCTGTAATG AAGAGAGTAT GTGTTCATTT CTGCTTTCAG GACCCAATTG GGATGAATCT 60 TTAAGTTTCT GGAAGTACCT GGACAGCTTC TTATCTCCAC ATATCCTTCA GCTTTCCTAT 120 GGATCTTTCA GTTCCATCTT CAGTGATGAT GAACAATATC CCTATCTCTA TCAGATGGCC 180 CCAAAGGACA CATCTCTAGC ATTGGCAATG GTCTCCTTCA TACTTTATTT GAAATGGAAT 240 TGGATTGGCC TTGTCATCCC AGATGACGAT CAAGGAAACC AATTTCTTTT AGAGTTGAAG 300 AAACAGAGTG AAAACAAAGA AATTTGCTTT GCCTTTGTGA AAATGATATC TGTTGATGAA 360 GTTTCATTTC CACAAAAAC TGAAATATAC TACAAACAAA TTGTGAAGTC ATTAACAAAT 420 GTTATTATCA TTTATGGAGA AACATATAAT TTCATTGATT TGATCTTCAG AATGTGGGAA 480 CCTCCCATTT TACAGAGAAT ATGGATCACC ACAAAACAAT TGAATTTCCC TACCAGTAAG 540 ACAGACATAA GTCATGACAC ATTCTATGGA TCACTTACTT TTCTACCCCA CCATGGTGAG 600 ATTTCTGGCT TTAAAAATTT TGTACAGACA TGGTTCCATC TCAGAAACAC AGATTTATAT 660 CTAGTAATGC CAGAGTGGAA ATATATTAAC TCTGAAGACT CAGCATCTAA TTGTAAAATA 720 CTGAAGAACA GTTCATCTGA TGCCTCATTT GATTGGCTAA TGGAACAGAA GCTTGACATG 780 GCCTTTAGTG ATAATAGTCA TAACATATAT AATGTTGTGC ATGCCATAGC CCATGCCCTC 840 CATGAGATGA ATCTGCAACA GGCTGATAAT CAGGCAATAG ATAATGGAAA AGGAGCCAGT 900 TCTCACTGCT TGAAGGTAAA CTCCTTTCTA AGAAGGACCT ACTTCACTAA TCCTCTTGGG 960 GACAAAGTGT TTATGAAGCA AAGAGTAATA ATGCAGGATG AATATGACAT TGTTCACTTT 1020 GCGAATCTCT CACAACACCT TGGGATTAAG ATGAAGTTAG GAAAGTTCAG CCCATATTTA 1080 CCACATGGTC GACACTCTCA CTTATACGTA GACATGATTG AGTTGGCCAC AGGAAGAAGA 1140 AAGATGCCAT CCTCTGTGTG CAGTGCAGAT TGTAGTCCTG GATTCAGAAG ATTATGGAAG 1200

GAGGGAATGG	CAGCCTGCTG	TTTTGTTTGC	AGCCCCTGCC	CTGAAAATGA	AATTTCTAAT	1260
GAGACAAATA	TGGATCAATG	CGTGAATTGT	CCAGAATACC	AATATGCCAA	CACAGAACAG	1320
AACAAATGTA	TTCAGAAAGG	TGTCACCTTC	CTAAGCTATG	AAGACCCCTT	GGGGATGGCA	1380
CTTGCCTTAA	TGGCCTTCTG	CTTCTCTGCA	TTCACAGCTG	TGGTACTTTG	TGTCTTTGTG	1440
AAGCACCATG	ACACTCCTAT	TGTGAAGGCC	AATAACAGAA	GCCTCAGCTA	TCTATTACTC	1500
ATGTCACTCA	TGTTCTGTTT	TCTGTGCTCC	TTTTTCTTCA	TTGGCCTTCC	AAACAAAGTC	1560
ATCTGTGTCT	TACAGCAGAT	CACATTTGGA	ATTGTATTTA	CTGTAGCTGT	TTCCACAGTT	1620
CTGGCCAAAA	CAGTCACTGT	GGTTCTAGCT	TTCAAAGTCA	CAGACCCAGG	AAGAAGATTG	1680
AGATACTTCC	TTGTATCAGG	GACACTAAAC	TACATTATTC	CTATATGTTC	CCTACTCCAA .	1740
TGTGTTCTGT	GTGCAATCTG	GCTAGCAGTC	TCTCCTCCCT	TTGTTGATAT	TGATGAACAC	1800
TCTCAGCATG	GCCACATCAT	CATTGTGTGC	AACAAGGGCT	CAGTTACTGC	ATTCTACTGT	1860
GTCCTTGGAT	ACTTGGCCTG	CCTGGCACTG	GGAAGCTTCA	CTTTGGCTTT	CTTGGCCAAG	1920
AATCTGCCTG	ATGCATTCAA	TGAAGCCAAG	TTCTTGACCT	TCAGCATGCT	AGTGTTCTGC	1980
AGTGTCTGGG	TCACCTTCCT	CCCTGTGTAC	CATAGCACAA	AGGGCAAACA	CATGGTTGCT	2040
GTGGAGATCT	TCTCCATCTT	GGCATCCAGT	GCAGGGATGC	TTGAATGTAT	TTTTGTACCC	2100
AAGATTTATA	TCATTTTAAT	GAGACCAGAG	AGAAATTCTA	CCCAAAAGAT	CAGGGAAAAA	2160
TCATATTTC						2169

(2) INFORMATION FOR SEQ ID NO:73:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1889 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

GAATTCGGCT	TCTGCACCAA	ATGGCGACGA	AAGACACATC	TCTTTCACTT	GCCATTGTTT	60
CTTTGATGGT	TCATTTTAGG	TGGTCTTGGG	TTGGTCTAAT	TCTCCCAGAT	GACCACAAAG	120
GAAATAAAAT	ACTATCAGAT	TTTAGAAAGG	AGATGGAAAG	AAAAAGAATC	TGTACGGCTT	180
TTGTAAAAAT	GATTCCTGCC	ACATGGACTT	CATCTTTTGT	CAAATTCTGG	GAAAATATGG	240
ATGACACCAA	CATAATAATT	ATTTATGGTG	ACATTGATTC	TCTAGAAGGT	CTAATGCGAA	300
ATATTGGGCA	AAGGTTATTG	ACATGGCATG	TCTGGGTCAT	GAACATTGAA	CCCCATATTA	360
TTGAATATGA	TAATTATTTC	ATGTTAGATT	CATTCCATGG	AAGTTTAATT	TTTAAGCACA	420
ATTATAGAGA	GAATTTTGAG	TTTACCAAAT	TTATTCGAAC	AGTTAATCCT	AAAAAATACC	480
CAGAAGACAT	TTATCTCCCT	AAGATGTGGT	ATTTGTTCTT	CATGTGCTCA	TTTTCTGATA	540
TTAATTGTCA	AGTTTTGGAC	AGCTGTCAAA	CAAATGCTTC	TTTGGATATG	TTACCTAGTC	600
AGATATTTGA	TGTGGTCATG	AGTGAAGAGA	GCACAAGTAT	TTACAATGCT	GTGTACGCTG	660
TGGCTCACAG	CCTCCATGAG	ATGAGACTTC	AGCAACTTCA	AACACAACCG	TGTGAAAATG	720
AAGAAGGGAT	GGAGTTCTTT	CCATGGCAGC	TTAATACTTT	CCTGAAGGAT	ATTGAGGTGA	780
GAGTCAACAG	TTTAGACTGG	AGACAGAGAA	TAGATGCTGA	ATATGACATT	CTTAACCTCT	840
GGAATTTACC	AAAGGGTCTT	GGACTAAAAG	TGAAAATAGG	AAACTTTTAT	GCAAATGCTC	900
CCCAGGGTCA	ACAATTGTCT	TTATCTGAAC	AGATGATTCA	ATGGCCAGAA	ATATTTTCAG	960
AGATCCCTCA	GTCGGTGTGC	AGTGAGAGTT	GTGGGCCTGG	ATTCAGGAAA	GTAACCCTGG	1020
AGAATAAGGC	TATCTGCTGC	TACAATTGTA	CTCCCTGTGC	AGACAATGAG	ATTTCTAATG	1080
AGACAGATGT	AGACCAGTGT	GTGAAGTGTC	CAGAGAGTCA	TTATGCAAAT	ACAGAGAAGA	1140
GCAACTGCTA	TCAAAAGTCT	GTGAGCTTTC	TGGGCTATGA	AGACCCTTTG	GGGATGGCTC	1200
TAGCCAGCAT	AGCTTTGTGC	TTGTCTGCAC	TAACTGCCTT	TGTTATTGGC	ATATTTGTGA	1260
AACACAAAGA	CACTCCTATT	GTTAAGGCCA	ATAATCAAGC	TCTGAGTTAC	ACTTTGCTCA	1320
TCACACTCAA	ATTCTGTTTC	CTATGTTCTT	TGAACTTCAT	TGGTCAGCCC	AACACAGTTG	1380
CCTGCATCCT	TCAGCAGACC	ACCTTTGCAG	TTGCTTTCAC	TATGGCTCTT	GCCACTGTGT	1440
TGGCCAAAGC	TATCACTGTG	GTTCTTGCCT	TTAAGGTCAG	TTTTCCAGGG	AGAATGGTAA	1500
GATGGCTAAT	GATATCAAGG	GGTCCAAACT	ATATCATTCC	TATCTGCACC	CTGATCCAAC	1560
TTCTTCTTTG	TGGAATATGG	ATGGCAATAT	CTCCACCATA	CATTGACCAA	GATGCTCATA	1620
TTGAACATGG	TCACATCATC	ATTTTGTGCA	ACAAGGGCTC	AGCTGTTGCC	TTCCACTCTG	1680
TCCTGGGATA	CCTCTGCTTC	TTGGCCCTTG	GGAGTTATAC	CATGGCCTTC	TTGTCAAGAA	1740
ATTTGCCTGA	TACATTCAAC	GAATCCAAAT	TTATCTCACT	AAGTATGCTG	GTATTCTTCT	1800
GTGTCTGGAT			ACAGCACTAA	AGGGAAGGTC	ATGGTCGCCG	1860
TCGAGGTCTT	TTGCATCCAA	GCCGAATTC				1889

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1889 base pairs

 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

GAATTCGGCT	TCTGCATCAA	ATGGCGACGA	AGGACACATC	TCTTTCACTT	GCCATTGTTT	60
CTTTGATGGT	TCATTTTAGG	TGGTCTTGGG	TTGGTCTAAT	TCTCCCAGAT	GACCACAAAG	120
GAAATAAAAT	ACTATCAGAT	TTTAGAAAGG	AGATGGAGAG	AAAAAGAATC	TGTACGGCTT	180
TTGTAAAAAT	GATTCCTGCC	ACATGGACTT	CATCTTTTGT	CAAATTCTGG	GAAAATATGG	240
ATGACACCAA	CATAATAATT	ATTTATGGTG	ACATTGATTC	TCTAGAAGGT	CCAATGCGAA	300
ATATTGGGCA	AAGGTTATTG	ACATGGCATG	TCTGGGTCAT	GAACATTGAA	CCCCATATTA	360
TTGAATATGA	TAATTATTTC	ATGTTAGATT	CATTCCATGG	AAGTTTAATT	TTTAAGCACA	420
ATTATAGAGA	GAATTTTGAG	TTTACCAAAT	TTATTCGAAC	AGTTAATCCT	AAAAAATACC	480
CAGAAGACAT	TTATCTCCCT	AAGATGTGGT	ATTTGTTCTT	CATGTGCTCA	TTTTCTGATA	540
TTAATTGTCA	AGTTTTGGAC	AGCTGTCAAA	CAAATGCTTC	TTTGGATATG	TTACCTAGTC	600
AGATATTTGA	TGTGGTCATG	AGTGAAGAGA	GCACAAGTAT	TTACAATGCT	GTGTACGCTG	660
TGGCTCACAG	CCTCCATGAG	ATGAGACTTC	AGCAACTTCA	AACACAACCG	TGTGAAAATG	720
AAGAAGGGAT	GGAGTTCTTT	CCATGGCAGC	TTAATACTTT	CCTGAAGGAT	ATTGAGGTGA	780
GAGTCAACAG	TTTGGACTGG	AGACAGAGAA	TAGATGCTGA	ATATGACATT	CTTAACCTCT	840
GGAATTTACC	AAAGGGTCTT	GGACTAAAAG	TGAAAATAGG	AAACTTTTAT	GCAAATGCTC	900
CCCAGGGTCA	ACAATTGTCT	TTATCTGAAC	AGATGATTCA	ATGGCCAGAA	ATATTTTCAG	960
AAGTCCCTCA	GTCTGTGTGC	AGTGAGAGTT	GTAGGCCTGG	ATTCAGGAAA	GTATCCCTGG	1020
ATGATAAGGC	CATCTGCTGC	TACAAGTGCA	CTCCTTGTGC	CGACAATGAG	ATATCTAATG	1080
AGACAGATGT	AGACCAGTGT	GTGAAGTGTC	CAGAGAGTCA	TTATGCAAAT	ACAGAGAAGA	1140
GCAACTGCTT	CCCAAAATCT	GTGAGCTTTC	TGGCCTATGA	AGACCCCTTG	GGGATGGCTC	1200
TAGCCAGCAT	AGCTTTGTGC	TTATCTGCAC	TCACTGTCTT	TGTTATTGGC	ATCTTTGTGA	1260
AAAACAGAGA	CACTCCTATT	GTCAAGGCCA	ATAATCGGAC	TCTAAGTTAC	ATTTTGCTCA	1320
TCACACTCAC	CTTTTGTTTC	TTATGTTCTT	TGAACTTCAT	TGGTCAGCCC	AACACAGCTG	1380
CCTGCATCCT	TCAGCAGACC	ACCTTTGCAG	TTGCTTTCAC	TATGGCTCTT	GCCACTGTGT	1440
TGGCCAAAGC	TATTACTGTA	GTCCTTGCCT	TTAAGATCAG	TTTTCCAGGG	AGAATGTTAA	1500
GGTGGCTAAT	GATATCAAGG	GGTCCAAGAT	ACATCATTCC	TATCTGCACA	CTGATCCAGC	1560
TTCTTCTTTG	TGGAATATGG	ATGGCAACTT	CTCCACCATT	CATTGACCAA	GATGTTAATA	1620
CTGAAGATGG	ATACATCATC	CTTTTGTGCA	ACAAGGGCTC	AGCTGTTGCC	TTCCATTCAG	1680
TCCTGGGATA	CCTCTGTTTC	TTGGCCCTTG	GGAGTTATAC	CATGGCCTTC	TTGTCTAGAA	1740
ATTTGCCTGA	TACATTCAAT	GAATCCAAAT	TTCTGTCATT	CAGTATGCTG	GTGTTCTTCT	1800
GTGTCTGGGT	CACCTTTCTT	CCTGTCTACC	ACAGCACTAA	AGGGAAAGTT	ATGGTCGTCG	1860
TCGAAGTCTT	CTGCATCCAA	GCCGAATTC				1889

- (2) INFORMATION FOR SEQ ID NO:75:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 270 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

ATGAAGAAGC	TCTGTGCTTT	CACGATTTCA	TTGTTGTTTC	TGAAGTTTTC	TCTCATCTTG	60
TGCTGTTGGA	GTGAACCAAG	TTGCTTTTGG	AGGATAAAGA	ATAGTGATGA	TAATGACGGA	120
GATTTGCAAA	GGGAATGTCA	TTTTTACCTT	GGGGCAGCTG	ATACACCAGT	TGAAGATAAT	180
TTTTATAGTT	CACTTTTAAA	ATTTAGGTTT	TCTTTGGACC	ATTTAATCCT	AACCTACGCG	240
ACCATGACCG	GCTGCCCCAT	GTCCATCAGG				270

- (2) INFORMATION FOR SEQ ID NO:76:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1308 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

ATGAAGAAGC	TCTGTGCTTT	CACGATTTCA	TTGTTGTTTC	TGAAGTTTTC	TCTCATCTTG	60
TGCTGTTGGA	GTGAACCAAG	TTGCTTTTGG	AGGATAAAGA	ATAGTGATGA	TAATGACGGA	120
GATTTGCAAA	GGGAATGTCA	TTTTTACCTT	GGGGCAGCTG	ATACACCAGT	TGAAGATAAT	180
TTTTATAGTT	CACTTTTAAA	ATTTAGAATT	GCAGCAAGTG	AATATGAGTT	TCTTCTCGTA	240
ATGTTTTTTG	CTATCGATGA	GATCAACAGG	AATCCTTATC	TTTTACCCAA	CATAACTTTG	300
ATGTTCTCCT	TCATTGGTGG	AAACTGTCAG	GATTTATTGA	GAGTTATGGA	CCAAGCATAT	360
ACACAAATAA	ATGGACATAT	GAATTTTGTT	AATTATTTCT	GTTATTTAGA	TGATTCATGT	420
GCCATAGGTC	TTACAGGACC	ATCATGGAAA	ACTTCCTTAA	AACTGGCAAT	GCACTCTTCG	480
ATGCCACTGG	TTTTCTTTGG	ACCATTTAAT	CCTAACCTAC	GCGACCATGA	CCGGCTGCCC	540
CATGTCCATC	AGGTAGCCCC	CAAGGACACA	CATTTGTCCC	ATGGCATGGT	CTCCTTGATG	600
TTTCACTTTA	GATGGACTTG	GATAGGAATG	GTCATCTCAG	ATGATGACCA	GGGTATTCAG	660
TTTCTCTCAG	ATTTAAGAGA	AGAAAGCCAA	AGGCATGGGA	TCTGTTTAGC	TTTTGTTAAT	720
ATGATCCCAG	AAAACATGCA	GATATACATG	ACAAGGGCTA	CAATATATGA	TCAACAAATT	780
ATGACATCTT	CAGCAAAGGT	TGTTATCATT	TATGGTGAAA	TGAACTCTAC	TCTAGAAGTA	840
AGCTTTAGAA	GATGGGAAGA	GTTAGGTGCT	CGGAGAATCT	GGATCACAAC	CTCACAATGG	900
GATGTCATCA	CAAATAAAAA	AGACTTCACC	CTTAATCTCT	TCCATGGGAC	TATCACTTTT	960
GCACACCACA	GAGTTGAGAT	TCCTAAATTA	AATAAATTCA	TGCAAACAAT	GAACACTGCC	1020
AAATACCCAG	TAGATATTTC	TCATACTATA	TTGGAGTGGA	ATTATTTAA	TTGTTCAATA	1080
TCTAAGAACA	GCATTAGAAT	GCATCATATT	ACATTCAACA	ACACCTTGGA	ATGGACATCA	1140
CTGCACAACT	ATGATATGGC	GATGAGTGAT	GAAGGTTACA	GTTTATATAA	TGCTGTTTAT	1200
GCTGTGGCCC	ACACCTACCA	TGAATACATT	TTTCAACAAG	TAGAGTCTCA	GAAAAAGGCA	1260
AAACCCAAAA	GATATTTCAC	TGCTTGTCAG	CAGATATGGA	ACAGTGTG		1308

- (2) INFORMATION FOR SEQ ID NO:77:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1296 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

ATGAAGAAGC	TCTGTGCTTT	CACTATTTCA	TTTTTGTCTC	TGAAGTTTTC	TCTCATCTTG	60
TGCTGTTTGA	CTGAAGCAAG	TTGCTTTTGG	AGGATAAAGA	ATAGTGAAGA	TAGTGATGGA	120
GATTTGCAAA	GAGAATGTCA	TTTTTACCTT	TGGGTAATTG	ATAAACCTAT	TGAAGATAAT	180
TTTTATAATT	CAGTTTTAAA	TTTTAGAATA	TCAGCAAGTG	AATATGAGTT	TCTTCTGGTA	240
ATGTTTTTTG	CTACTGATGA	GATCAACAAG	AATCCTTATC	TTTTACCCAA	CATAACTTTG	300
ATATTCAGCA	TCGTTGGTGG	TCACTGTCAT	GATTTATTGA	GAGGTCTGGA	TCAATCATAT	360
ACACAAATAA	ATGGACGTGT	GAATTTTGTT	AATTATTTCT	GTTATTTAGA	TGATTCATGT	420
AACATAGGCC	TTACAGGACC	ATCATGGAAA	AAATCCTTAA	AACTGGCAAT	GGATTCTTCA	480
ATACCAATGG	TTTTCTTTGG	ACCATTTAAT	CCTAACCTAC	GCGACCATGA	CCGGCTGCCC	540
CATGTCCATC	AGGTAGCCCC	CAAGGACACA	CATTTATCCC	ATGGCATGGT	CTCCTTGATG	600
TTTCATTTTA	GATGGACTTG	GATAGGACTG	GTCATCTCAG	ATGATGACCA	GGGTATTCAG	660
TTTCTCTCAG	ATTTAAGAGA	AGAAAGCCAA	AGGCATGGGA	TCTGTTTAGC	TTTTGTTAAT	720
ATGATCCCAG	AAAACATGCA	GATATACATG	ACAAGGGCTA	CAATATATGA	TAAACAAATT	780
ATGACATCTT	CAGCAAAGGT	TGTTATCATT	TATGGTGAAA	TGAACTCTAC	TCTAGAAGTA	840
AGCTTCAGAA	GATGGGAAGA	TTTAGGTGCT	CGGAGAATCT	GGATCACAAC	CTCACAATGG	900
GATATCATAT	TAAATAAAA	AGAATTCACT	CTTAATCTCT	TCCATGGCCC	TATCACTTTT	960
GCACACCACA	AAGTTGAGAT	TCCTAAATTA	AGGAATTTTA	TGCAAACAAT	GAACACTGCC	1020
AAATACCCAG	TAGATATTTC	TCATACTATA	CTGGAGTGGA	ATTATTTTAA	TTGTTCAATC	1080
TCTAAGAACA	GCAGTAAAAT	GGATCTTTTT	ACATCCAACA	ACACATTGGA	ATGGACAGCA	1140
CTGCACAACT	ATGATATGGC	CATGAGTGAT	GAAGGTTACA	ATTTGTATAA	TGCTGTTTAT	1200
GTTGCGGCCC	ACACCTACCA	TGAACACATT	CTTCAACAAG	TAGAGTCTCA	GAAAAAGGTA	1260
GAÁCACAACA	GATATTTCAC	TGTTTGTCAG	CAGATA			1296

(2) INFORMATION FOR SEQ ID NO:78:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1521 base pairs
- (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

ATGAAGAAGC T	المستعماليات المستعمليات	CA OMA MMMCA	mmmmamamama			
MCCMCMMAC 1	CIGIGCIII			TGAAGTTTTC	TCTCATCTTG	60
	TGAAGCAAG			ATAGTGAAGA	TAGTGATGGA	120
	AGAATGTCA			ATAAACCTAT	TGAAGATAAT	180
	AGTTTTAAA		TCAGCAAGTG	AATATGAGTT	TCTTCTGGTA	240
ATGTTTTTTG C	TACTGATGA	GATCAACAAG	AATCCTTATC	TTTTACCCAA	CATAACTTTG	300
ATATTCAGCA T	CGTTGGTGG	TCACTGTCAT	GATTTATTGA	GAGGTCTGGA	TCAATCATAT	360
ACACAAATAA A	TGGACGTGT	GAATTTTGTT	AATTATTTCT	GTTATTTAGA		420
AACATAGGCC T	TACAGGACC	ATCATGGAAA			GGATTCTTCA	480
				GCGACCATGA		540
CATGTCCATC A	GGTAGCCCC	CAAGGACACA	CATTTATCCC	ATGGCATGGT	CTCCTTGATG	600
TTTCATTTTA G				ATGATGACCA		660
TTTCTCTCAG A	TTTAAGAGA	AGAAAGCCAA	AGGCATGGGA	TCTGTTTAGC	TTTTGTTAAT	720
ATGATCCCAG A	AAACATGCA	GATATACATG	ACAAGGGCTA	CAATATATGA	TABACAAATT	780
ATGACATCTT C	AGCAAAGGT	TGTTATCATT		TGAACTCTAC		840
AGCTTCAGAA G	ATGGGAAGA	TTTAGGTGCT		GGATCACAAC		900
GATATCATAT T				TCCATGGCCC		960
GCACACCACA A				TGCAAACAAT		
		ТСАТАСТАТА	CTGGAGTGGA	ATTATTTTAA	GAACACTGCC	1020
TCTAAGAACA G				ACACATTGGA-		1080
						1140
		CAIGAGIGAT		ATTTGTATAA		1200
GAACACAACA G		TGAACACATT		TAGAGTCTCA		1260
				CCTTGATGAA	AACCAGGGTA	1320
				GGGAAAATCA	GTGTACAGAG	1380
				GATTAAAATT	GAAAATAGGA	1440
		AAAGAGTCAA	CAACTTCATA	TATCTGATGA	TTTGGAATGG	1500
GCCATGGGAG G	AACATCAAT	A			•	1521

- (2) INFORMATION FOR SEQ ID NO:79:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 933 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: CDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

ATGAAGCAGC	TCTGCACTTT	CACTATTTCA	TTGTTGTTTC	TGAAGTTTTC	TCTCATCTTG	60
TGCTGTTGGA	GTGAACCAAG	CTGCTTTTGG	AGGATAAAGA	AGAGTGAAGA	TAATGATGGA	120
GATTTACAAA	GGGAGTGTCA	TTTTTACCTT	TGGAAAACTG	ATGAACCTAT	TGAAGATAGT	180
TITTATAATT	ATGATTTAAG	TTTTAGAATT	GCAGGAAGTG	AATATGAGCT	TCTTCTGGTA	240
ATGTTTTTTG	CTACTGATGA	GATCAACAAG	AATCCTTATC	TTTTACCCAA	CATGAGTTTG	300
ATGTTCTCCA	TCATTGGTGG	AAACTGTCAT	GATTTATTGA	GAAGTCTGGA	TCAAGAATAT	360
GCACAAATAG	ATGGACATAT	GAATTTTGTT	AATTATTTCT	GTTATTTAGA	TGATTCATGT	420
GCCACAGGCC	TTACAGGACC	ATCATGGAAA	ACATCCTTAA	AACTGGCAAT	GCATTCTTCA	480
ATGCCACTGG	TTTTCTTTGG	ACCATTTAAT	CCTAACCTAC	GCGACCATGA	CCGGCTGCCC	540
CATGTCCATC	AGGTAGCCCC	CAAGGACACA	CATTTGTCCC	ATGGCATGGT	CTCCTTGATG	600
TTTCATTTTA	GGTGGACTTG	GATAGGACTG	GTCATCTCAG	ATGATGATCA	GGGTATTCAG	660
TTTCTCTCAG	ATTTAAGAGA	AGAAAGCCAA	AGGCATGGGA	TCTGTTTGGC	יייע עיייינאויירייי	720
ATGATCCCAG	AAAACATGCA	GATATACATG	ACAAGGGCTA	CAATATATGA	TACACAAATT	780
ATGACATCTT	CAGCAAAGGT	TGTTATCATT	TATGGTGACA	TGAACTCTAC	TCTAGAAGGA	840
						940

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AGCTTTAGAA GATGGGAAGA GTTAGGTGCT CGGAGAATCT GGATCACAAC CACACAATGG 900 GATGTCATCA CAAATAAAAA AAGACTTCAC CCT 933

- (2) INFORMATION FOR SEQ ID NO:80:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1236 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

GCAAGTTGCT	TTTGGCGGAT	AAAGAATAGT	GAAGATAATG	ATGGAGATTT	GCAAAGGGAA	60
TGTCATTTTT	ACCTTGGGGC	AGTTGATAAA	CCAATTGAAG	ATAATTTTTA	TAATTCACTT	120
TTAAAGTTTA	GAATTGCAGC	AAGTGAATAT	GAGTTTCTTC	TGGTAATGTT	TTTTGCTACT	180
GATGAGATCA	ACAAGAATCC	TTATCTTTTA	CCCAACATAA	CTTTGATGTT	CTCCATCATT	240
GGTGGAAACT	GTCATGATTT	ATTGAGAGGT	TTGGATCAAG	CATATACACA	AATAAATGGA	300
CATATGAATT	TTGTTAATTA	TTTCTGTTAT	TTAGATGATT	CATGTGCCAT	AGGTCTTACA	360
GGACCATCAT	GGAAAACATC	CTTAAAACTG	GCAATGCATT	CTTCAATGCC	ACTGGTTTTC	420
TTTGGATCAT	TTAATCCTAA	CCTACATGAC	CATGACCGGC	TGCACCATGT	CCATCAAGTA	480
GCCACCAAGG	ACACACATTT	GTCCCATGGC	ATTGTCTCCT	TGATGTTTCA	TTTTAGATGG	540
ACTTGGATAG	GACTGGTCAT	CTCAGATGAT	GACAAGGGTA	TTCAGTTTCT	CTCAGATTTA	600
AGAGAAGAAA	GCCAAAGGCA	TGGGATCTGT	TTAGCTTTTG	TTAATATGAT	CCCAGAAAAC	660
ATGCAGATAT	ACATGACAAG	GGCTACAATA	TATGATAAAC	AAATTATGAC	GTCTTTAGCA	720
AAAGTTGTTA	TCATTTATGG	TGAAATGAAC	TCTACACTAG	AAGTAAGCTT	TAGAAGATGG	780
GAAAATTTAG	GTGCTCGGAG	AATCTGGATC	ACAACCTCAC	AATGGGATGT	CATCACAAAT	840
TAAAAAAGAAT	TCACCCTTAA	TCTCTTCCAT	GGGACTATTA	CTTTTGCACA	CCGCAGATTT	900
GAGATTCCTA	AATTTAAAAA	ATTTATGCAA	ACAATGAACA	CTGCCAAATA	CCCAGTAGAT	960
ATTTCTCATA	CTATATTGGA	GTGGAATTAT	TTTAATTGTT	CAATCTCTAA	GAACAGCAGT	1020
AAAATGGATC	ATATTACATT	CAACAACACA	TTGGAATGGA	CAGCACTGCA	CAACTATGAT	1080
ATGGTGATGA	GTGATGAAGG	TTACAATTTG	TATAATGCTG	TTTATGCTGT	GGCCCACACC	1140
TACCATGAAC	ATATTTTTCA	ACAAGTAGAG	TCTCAGAAAA	AGGCAAAACC	CAAAAGATTT	1200
TTCACTGTTT	GTCAGCAGCA	GATATGGAAC	AGTGTG			1236

- (2) INFORMATION FOR SEQ ID NO:81:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2412 base pairs

 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

ATGTTCATTT	TCATGGAAGT	CTTCTTCCTC	CTTAATATTA	CACTTCTCAT	GGCCAATTTC	60
ATTGATCCCA	GGTGCTTTTG	GAGAATAAAT	TTGGATGAAA	TAATGGATGA	ATATTTGGGA	120
TTATCTTGTG	CTTTCATCCT	GGCAGCAGTT	CAGACACCCA	TTGAAAATGA	TTATTTCAAC	180
AAGACTCTTA	ATGTTCTAAA	AACAACTAAA	AACCACAAAT	ATGCTTTGGC	ATTGGTGTTT	240
GCAATGGATG	AAATCAACAG	AAATCCTGAT	CTTTTACCAA	ATATGTCTTT	GATTATAAGA	300
TACACTTTGG	GCCGTTGTGA	TGGAAAAACT	GTAATACCTA	CACCATATTT	ATTTCGTAAA	360
AAAAAAGAAA	GCCCTATCCC	TAATTATTTC	TGTAATGAAG	AGACTATGTG	TTCCTATCTG	420
CTTACAGGAC	CCCATTGGGA	GGTATCTTTA	GGTTTCTGGA	AGCACATGAA	CAGCTTCTTA	480
TCTCCACGŢA	TCCTTCAGCT	TACCTATGGA	CCTTTCCACT	CCATCTTCAG	TGATGATGAA	540
CAATATCCCT	ATCTCTATCA	GATGGCCCCA	AAGGACACAT	CTCTAGCATT	GGCAATGGTC	600
TCCTTCATAC	TTTACTTTAG	CTGGAACTGG	ATTGGCCTTG	TCATTCCAGA	TGATGACCAA	660
GGAAACCAAT	TTCTTTTAGA	GTTGAAGAAA	CAGAGTGAAA	ACAAGGAAAT	TTGCTTTGCC	720
TTTGTGAAAA	TGATCTCTGT	TGATGATGTT	TCATTTCCAC	AAAATACTGA	AATGTACTAC	780
AACCAAATTG	TGATGTCATC	CACAAATGTT	ATTATCATTT	ATGGAGAAAC	ATACAATTTC	840
ATTGATTTGA	TCTTCAGAAT	GTGGGAACCT	CCCATTTTAC	AGAGAATATG	GATCACCACA	900
AAACAATTGA	ATTTCCCTAC	CAGGAAAAA	GACATAAGTC	ATGGCACATT	CTATGGATCA	960

CTTACTTTTC	TACCCCACCA	TGGTGTGATT	TCTGGTTTTA	AAAATTTTGT	ACAGACATGG	1020
TTCCATCTCA	GAAACACAGA	TTTATATCTA	GTAATGCAAG	AGTGGAAATA	CTTTAACTAT	1080
GAAGACTCAG	CATCTACCTG	TAAAATACTG	AAGAACAATT	CATCTAATGC	CTCATTTGAT	1140
TGGCTAATGG	AACAGAAGTT	TGACATGACC	TTTAGTGAGA	ATAGTCATAA	CATATACAAT	1200
GCTGTGCATG	CCATAGCCCA	TGCCCTCCAT	GAGATGAATC	TGCAACAGGC	TGATAATCAG	1260
GCAATAGACA	ATGGGAAAAA	GGAGCCCAGT	TCCTCCCACT	GCTTGAAGGT	AAACTCCTTT	1320
CTAAGAAGGA	TTTACTTCAC	TAATCCTCCT	GGGGACAAAG	TGTTTATGAA	GCAAAGAGTA	1380
ATAATGCACG	ATGAATATGA	CATTGTTCAC	TTTGTGAATC	TCTCACAACA	CCTTGGGATT	1440
AAGATGAAGT	TAGGAAAGTT	CAGCCCATAT	TTACCACATG	GTCGACACTC	TCACTTATAT	1500
GTAGACAGGA	TTGAGTTGGC	CACAGGAAGA	AGAAAGATGC	CATCCTCTGT	GTGCAGTGCT	1560
GATTGTAGTC	CTGGATTCAG	AAGATTATGG	AAGGAGGGAA	TGGCAGCCTG	CTGTTTTGTT	1620
TGCAGCCCCT	GCCCTGAAAA	TGAAATTTCT	AATGAGACAA	CTGTGGTACT	TTGTGTCTTT	1680
GTGAAGCATC	ATGACACTCC	TATTGTGAAG	GCCAATAACA	GAAGCCTCAG	CTACCTATTA	1740
CTCATGTCAC	TCATGTCCTG	TTTTCTGTGC	TCCTTTTTCT	TCATTGGCCT	TCCAAACAGA	1800
GCCATCTGTG	TCTTACAGCA	AATCACATTT	GGAATTGTAT	TCACTATGGC	TGTTTCCACA	1860
GTTCTGGCCA	AAACAGTCAC	TGTGGTTCTG	GCTTTCAAAG	TCACAGACCC	AGGAAGAAGA	1920
TTGAGAAACT	TCCTGGTATC	AGGAACACCC	AACTACATTA	TTCCCATATG	TTCCCTACTC	1980
CAATGTGTTC	TGTGTGCAAT	CTGGCTAGCA	GTTTCTCCTC	CCTTTGTTGA	TATTGATGAA	2040
CACACTCTCC	ATGGCCACAT	CATCATTGTG	TGCAACAAGG	GCTCAGTTAC	TGCATTCTAC	2100
TGTATCCTAG	GATACTTGGC	CTGCCTGGCA	CTTGGAAACT	TCTCTGTGGC	TTTCTTGGCC	2160
AAGAATCTGC	CTGACACATT	CAATGAAGCC	AAGTTCTTGA	CCTTCAGCAT	GCTAGTGTTC	2220
TGTAGTGTCT	GGGTCACCTT	CCTCCCTGTC	TACCATAGCA	CCAAGGGCAA	ACACATGGTT	2280
GCTGTGGAGA	TCTTCTCCAT	CTTGGCATCC		TCCTTGGATG	TATATTTGTA	2340
CCCAAGATTT	ATATCATTTT	AATGAGACCA	GAGAGAAATT	CGACCCAAAA	GATCAGGGAA	2400
AAATCATATT	TC					2412

- (2) INFORMATION FOR SEQ ID NO:82:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 381 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

ATGTTCATTT	TCATGGGAGT	CTTCTTCCTC	CTTAATATTA	CACTTCTCAT	GGCCAATTTC	60
ATTAATCCCA	GGTGCTTTTG	GAGAATAAAT	TTGGATGAAA	TAACGGATGA	ATATTTGGGA	120
TTATCTTGTA	CTTTCATCCT	GGCGGCAGTT	CAGACACCCA	CTGAAAAAGA	TTATTTCAAC	180
AAGACTCTTA	ATGTTCTAAA	AACAACTAAA	AACCACAAAT	ATGCTTTGGC	ATTGGTGTTT	240
GCAATGGATG	AAATCAACAG	AAATCCTGAT	CTTTTACCAA	ATATGTCTTT	GATTATAAGA	300
TACACTTTGG	GCCTTTGTGA	TGGAAAAACT	GTAACACCTA	CACCATATTT	ATTTCATAAA	360
AAAAAAACAA	AGCCCTATCC	C				381

- (2) INFORMATION FOR SEQ ID NO:83:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 228 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

ATGAAAAACC TGTGTGTTTT (CACTCTTTCC	TTTTTCCTCC	TGGAGTTTTC	TCTGATCTTG	60
TGCCATTTGA CTGAACCCAT	TTGCTTTTGG	AGGATAAATA	ATAATGAAGA	TAATGATGGA	120
GATTTGAGAA GTGACTGTGG	TTTTTTCCTT	GCAGCAGTTG	AGGGACCTAC	TGACGACTCT	180
TATAATATCT CTGATCTTAG	GTTTTCTTTG	GACCATTTAA	TCCTAAGC		228

(2) INFORMATION FOR SEQ ID NO:84:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1644 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

ATGTTAGAAT TGGCCCATGG	CACTCTGACT	TTCTCACCCC	ATCATGGGGA	GATTTCTGAT	60
TTCACAAATT TTATGCAGGA	AGTCACCCCT	ATCAAGTACC	CAGAAGACAT	TTTTCTTCAC	120
ATCTTGTGGA ACCAGTATTT	CAATTGTCCA	CTTTTGCATT	CTGAGTGTAA	AATCTTTGAA	180
AACTGTATAC CCAATGCCTC	TTTGGAATTG	TTGCCAGGGG	GTGTTTTTGA	GCTGGTCATG	240
ACTGAAGAGA GTTACAATGT	GTACAATGCT	GTGTATGCAG	TGGCCCACAG	TCTCCATGAG	.300
AAGGCTCTCC ATCAAGTAGA	AATTCAACCA	CAGGATAATA	AAGATAGGAC	TATATTATTT	360
CCTTGGCAGC TTCACCCTTT	TCTGAAGAAC	ATTCAGCTGA	TAAATTCTGT	TGGTGATCGT	420
GTGATTCTGG ACTGGAAAAA	GAAGACGGAT	ACAGAGTATG	ATATTTCCAA	TATTTGGAAT	480
TTCCCAACAG GTCTTTCCTT	ATTAGTGAAA	GTGGGTACAT	TTGCTCCAAG	TGCTCCCAAG	540
GGGGAACAAC TTTCGATATC	TGAACACACA	ATTAACTGGC	CCATAGGATT	TACAGAGATT	600
CCAAAGTCTG TATGCAGTGA	GAGCTGCAGT	CCTGGACACA	GGAAAGTCAT	CCTGGAGAGC	660
AAGCCTGCCT GTTGCTTTGA	CTGCACTCCT	TGCCCAGATA	AAGAGATTTC	CAACGAGACA	720
GATGTGGGTC AGTGTGTGAA	GTGTCCTGAA	TCTCATTATG	CAAATACAGA	GAAGAGTCAC	780
TGCCTGAAGA AGACTATGAC	CTTTCTGGAT	TATAATGATT	CCTTGGGGAC	GGGACTCACA	840
CTCATGTCTC TGGGATTCTT	TGTTGTCACA	GGTCTTGTTA	TTGGGGTTTT	TATAATCCAC	900
AGAAACACTC CAATTGTGAA	GGCCAATAAT	AGATCTCTCA	GTTATATCCT	GCTCATCACT	960
CTCACTCTCT GTTTCCTTTG	TCCCTTGCTC	TTCATTGGGC	TTCCAAACAC	AGCCACATGT	1020
ATCCTACAGC AGAACTTGTT	TGGACTTCTC	TTCACTGTGG	CTCTATCCAC	AGTGTTGGCC	1080
AAAACTATCA CTGTAGTTAT	GGCATTCAAG	ATTACTGCTC	CAGGAAGAAA	GACAAGATGG	1140
TTGCTGATAT TAAGAGCCCC	TCAGTTCATC	ATTCCACTTT	GTGCCCTGAT	GCAAATCCTT	1200
TTCTCTGGGA TATGGCTGGG	AACATCTCCT	CCATTTGTTG	ACATGGATGC	TCACTCTGAA	1260
CATGGGCACA TCATCATTCT	ATGCAACAAG	GGCTCAGCTA	TTGGCTTCTA	CTGTACTCTG	1320
GCCTACCTGG GAGTCATGGC	CTTTGGTAGT	TACCTCTTGG	CTTTCATGTC	CAGGAATCTT	1380
CCTGACACAT TTAATGAATC	CAAGGCCCTG	GCTTTCAGCA	TGCTGATGTT	CTGCAGTGTC	1440
TGGGTCACAT TCCTCCCTGT	CTACCACAGC	ACCACTGGGA	AGGTCAGGGT	GGCTATGGAA	1500
ATGTTTTCTA TCTTGGCTTC	CAGTGCAAGC	ATTCTAACCC	TAATCTTTGT	CCCTAAGTGC	1560
TACATTGTTT TGTTCAGACC	AGAGAGGAAC	ATACTTCCTC	TAAACAGAGA	AAAAAGACAG	1620
CATAGGAGTA AAAATTCTGA	AACA				1644

- (2) INFORMATION FOR SEQ ID NO:85:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2304 base pairs

 - (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

ATGGAGGAAA	TCAACAGGAA	CCCTGATCTT	TTACCAAATA	TGTCTTTGGT	TATAAAACAT	60
ACTTTGAGCT	ATTGTGATGG	AAATACTGCA	GACCATATAT	TTAAAGAAAA	ATTTTATAAG	120
CCTTTACCTA	ATTATGTCTG	TAATGAAGAG	ACTATGTGTT	CATTTATGCT	TATAGGGCTG	180
AATTGGGTAT	TGTCTCTAAC	ACTTTTTAAA	GACTTGGACA	TCTTCTCATT	TCCACGTTTC	240
CTTCAAATTT	CCTATGGACC	TTTCCATTCC	ATCTTCAGTG	ATAATGAACA	ATTTCCATAT	300
CTCTATCAGA	TGACCCCAAA	GGACACATCA	CTAGCATTGG	CAATTGTCTC	CTTCTTACTT	360
TACTTCAATT	GGAACTGGGT	TGGGCTTGTC	ATCTCTGATA	ATGATGAAGG	CAATCAATTT	420
CTCTCAGAGT	TGAAAAAAGA	GACCCAAAAC	AAGGAAATTT	GCTTTGCCTT	TGTTAACATG	480
ATGTCAATCC	ATGAGCATTC	ATCTTATCAA	AAAACTGAAA	TGTACTACAA	TCAAATAGTG	540
ATGTCATCAA	CAAATATTAT	TATCATTTAT	GGGAAAACAA	ACAGTATCAT	TGAATTGAGC	600
TTCAGAATGT	GGGTATCTCC	AGTTATACAG	AGGATTTGGG	TCACAAACTC	AGAGTTGGAT	660
TTCCCGACAA	GTATGAGAGA	CTTCACTCAT	GGCACATTCT	ATGGGACTCT	GACATTTCTA	720
CACCACCATG	GTGAGATTTC	TGGATTTACA	AATTTTTTCG	AGACATGGGA	CCATCTCAGA	780
AGCAGAGATT	TAAATCTATT	AATACCAGAG	TGGAAGTACT	TTAGCTATGA	TGCCTCAGGA	840

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TCTAACTGTA	AAATATTGAG	GAACTATTCA	TCCAATGCCT	CATTGGAATG	GATAACAGAA	900
CAGAAGTTTC	ACATGGCCTT	TAATGATTAT	AGTCATAGTA	TATATAATGC	TGTGTATGCC	960
ATGGCCCATG	CCCTCCATGA	GACTAATCTG	CAAGAGGTTG	ATAATAAGGA	AATAAGAAAT	1020
GGGAAAGGAG	CAAGTACTCA	CTGCTTGAAG	GTAAACTCAT	TTCTCAGAAA	GACCCACTTT	1080
ACTAATTCTC	ATGGAGAGAG	AGTGATTATG	AAACAGAGAG	TGAGAGTACA	GGAAGACTAT	1140
GACATTGTTC	ACATTCAGAA	TTTCTCACAA	CACCTTCGGA	TTAAGATGAA	GATAGGAAAG	1200
TTCAGCCCAT	ATTTTACACA	TGGTGGACCC	TTTCACTTAT	ATGAAGACAT	GATTCAGTTG	1260
GCCACAGGAA	GTAGAAAGAT	GCCGTCCTCT	GTGTGCAGTG	CAGATTGTAG	TCCTGGATTC	1320
AGAAAATCCT	GGAAGGAGGG	AATGGCCCCC	TGCTGTTTTA	TTTGCAGCCT	GTGCCCTGAA	1380
AATGAAATTT	CTAATGAGAC	AAATATGGAT	CAATGTGTGA	ATTGTCCAGA	ATACCAATAT	1440
GCCAACACAG	AAAAGAACAA	ATGCATTCAG	AAAGACGTGA	TTTTTCTAAG	CTATGAAGAC	1500
CCCTTGGGAA	TGGCTCTTGC	CTTAATTGCC	TTCTGTTTGT	CTGCATTCAC	AGCTGTGGTA	1560
CTTTGGGTCT	TTGTGAAGCA	CCATGACACT	CCTATTGTGA	AGGCCAATAA	CAGAATCCTC	1620
AGCTACATAT	TAATCATGTC	ACTAATGTTC	TGTTTTCTCT	GCTCCTTTTT	CTTCATTGGC	1680
CATCCTAACA	GAGGTACCTG	TATCTTACAG	CAAATCACAT	TTGGCATTGT	ATTCACTGTG	1740
GCTGTTTCCA	CAGTTCTGGC	CAAAACAATC	ACTGTCATTC	TTGCTTTCAA	ACTCAGAGAC	1800
CCAGGGAGAA	GTTTAAGAAA	CTTCCTGGTA	TCTGGTGCAC	CCAACTACAT	TATTCCTATA	1860
TGTTCCTTAT	TGCAATGTAT	TCTGTGTGCA	ATTTGGCTAG	CAGTTTCTCC	TCCTTTTGTT	1920
GATATTGATG	AACATTCTGA	GCATGGCCAC	ATCATGATTG	TGTGCAACAA	GGGCTCCATT	1980
ATGGCATTCT	ACTGTGTCCT	AGGATACTTG	GCCTGCCTGG	CGCTTGGAAG	CTTCACTACA	2040
GCTTTCTTGG	CAAAGAATCT	GCCAGACACA	TTCAACGAAG	CCAAGTTCTT	GACCTTCAGC	2100
ATGCTAGTGT	TCTGCAGTGT	CTGGGTCACC	TTTCTCCCTG	TGTACCATAG	CACAAGGGGC	2160
AGGGTCATGG	TTGCTGTTGA	GATCTTCTCT	ATCTTGGCAT	CCAGTGCAGG	GATGTTTGGA	2220
TGCATCTTTG	CACCCAAAAT	CTACATCATA	TTAATGAAAC	CAGAAAGAAA	TTCTATACAA	2280
AAGTTCAGGG	AGAAATCATA	TTTC				2304

(2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2001 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

ATGGCTCCTA AGGACACATC TCTGGCACTG GCCATGGTTT CTTTGTTTGT CCATTTCAGC TGGAACTGGG TAGGAGCTGT TGTTTCAGAT GATGACCCAG GTTATGAATT TATCTTGGAA 120 TTGAGAAGAG AAATGCAAAG GAACAATTTT TGTTTAGCAT TTGTGAGTAT CATTGTTAGT 180 GATGACAATT TATTTCTGAA AAGGTATAAT ATCTATTACA ACCAGATCAA GATGTCATCA 240 GCAAAAGTTG TTATCATTTA TGGAGACAAA GACTCTCCTC TACAGGTGAA CTTTAGACTA 300 TGGAATTTAT TTGATATCCA AAGAATCTGG GTCACTACTT CACAGTGGGA TATGATCATA AATAATGGAA AATTCCTCCT TAATTCCTTC TATGGGACTC TCAGTTTTTC ACATCACTAT TCTGAATTAT CTGGTTTTAA AACATTTATC CAGACAGCAT ACCCTTCAAA CTACAGTGAT 360 420 480 GACTTTTCTC TTGGTATATT ATGGTGGGTG TATTTTAATT GTTCTTTGTC ATTATCTGAA 540 TGTAAGAATC TGCAAAATTG TCCAAAGGAA AACATATTTA GATGGTTATA CAGGCACCAT TTTGAAATGT CTTTGAGTGA TACTACTTAT GACCTATATA ATTCTATGTA TGCTGTGGCT 660 TACACACTCC AACAGATGCT TCTGAAACAA GCAGATACAT GGCAAATAGA TGATGGAAAA 720 GAACCAGAAT TTGACTCTTG GCAGATGCTC TCTTTCCTGA GAAATATCCA ATTTATAAAC 780 CCTGTTGGTG ACAAAGTGAA CCTGAATCAT GAAGAAAAAC TGGATACAAA GTATGAGATT CACCAGACTT TGACTTTTTT GCCAAATCCT GTATTTAAGC TGAAAATAGG AACATTTTCC 900 CAAAACTTAT CACATGGTCG ACAATTATAT ATGTTGAAAG AAATGATAGA GTGGAACACA GGCCACCAAC AGTCTCCAAC CTCAGTTTGC AGTATTCCTT GTAGTCCAGG ATTCAGAAAA 960 1020 TCCCCTCAGC TGGGAAAGCC TGTTTGCTGT TTTGATTGTA CACCCTGCCC AGAAAATGAA 1080 ATTTCCAACA TGACAAACAT GAATCAATGT ATCAAGTGTC TAAATGATCA GTATGCCAAT 1140 CCTGGAGGAA CTCGCTGCCT CAAAAAAGTT ATTGTATTCC TGGGTTATGA AGATCCATTG GGAATGTCTC TGGCTATCTT GGCTCTGTGC TTCTCTGCTC TCACAGCTTT TGTACTTAGT 1200 ATCTTTTTGA AGCACCAAGA AACACCCACT GTCAAGGCCA ATAATAGAAC TCTCAGCTAT 1320 GTTCTACTCA TCTCCCTCAT CTCTTGTTTT CTCTGCTCCT TGCTCTTCAT TGGTCATCCC AGCTTTACCA CATGTATCAT GCAGCAGACC ACATTTGCTG TTGTGTTCAC TGTAGCTGCA TCTACTGTCT TGGCCAAAAC AATTATTGTA ATATTGGCCT TCAAGGTTAC TAATACAAGT 1440 1500 AGAAAAATGA GGTGGCTGCT GGTATCAGGG GCACCTAAAT TCATCATTCC AATTTGCACA 1560 ATGATTCAAC TGATTCTCTG TGGAATTTGG CTGGGTACTT CTCCTCCATT TGTTGATGCT 1620 - 189 -

GATGGACATG TTGAAAAAGG	CCACATTTTG	ATTTTCTGTA	ACAAAGGTTC	AATTCTTGCT	1680
TTCTATTGTG TCCTGGGATA	CTTAGTCTCC	ATTGCCATTG	CAAGTTTCAC	CCTTGCATTC	1740
TTCGCCAGAA ATCTGCCCGA	CACATTCAAT	GAAGCCAAGT	TCCTAACATT	CAGTATGCTA	1800
GTATTTTGCA GTGTCTGGGT	CACCTTTCTT	CCTGTCTATC	ATAGCACCAA	GGGCAAGTCT	1860
ATGGTGGCTG TGGAAGTTTT	CTGTATATTG	GCCTCTAGTG	CAGGGCTGCT	TTTTTGCATC	1920
TTTGCACCAA AGTGCTTCAT	TATTTTGTTA	AGACCTGAGA	AAAAATCTTT	TCAGAAGTTT	1980
CAGAATATAC ATTCTAAAAT	T				2001

(2) INFORMATION FOR SEQ ID NO:87:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 2598 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

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ATGTCCAGGC	TCAGAGCAGG	AAAAAATATG	CTCACCTTCA	TTTTACTCTT	CTTTCTCCTG	60
AACATTCCAC	TTTTTGTGCC	TAGTTTTATT	TATCCCAGGT	GCTTTTGGAG	TATGAAGAAG	120
AATGAATATC	AGGATAGAAA	CCTGGGAACA	GGTTGTATGT	TCTTTATTCT	AGCAGTGCAA	180
		TTTCAGTCAT			TACTGAAAAC	240
CAAAAGTATC	CTCTCACCTT	GGCTTTTTCC	ATGAATGAAA	TCAACAACAA	CCCTGATCTT	300
		ATTTACATTC			GGAATCCCAC	360
CACAAAAGAT	TATTTAATTT	TTCTTTAAAA	AATCATGAAA	TTCTCCCTAA	TITTATCTGT	420
ACAAAAGACA	TCAAGTGTGG	AGTGGTACTT	ACCGGACTTA	GTTTGGTAAC	AACTGTGACA	480
		TTTCATATTT				540
		TCATGAAAAT				600
		TCTCGTCTCC				660
GGGTTGGCCA	TCTCAGACAA	TGATCAAGGC	ATACATTTTC	TCTCTTATTT	GAGAAGAGAG	720
ATGGAAAAA	ATACAGTCTG	CTTTGCCTTT	GTCAACATTA	TTCCAGTCAA	TATGAATTTA	780
TACATGTCAA	GAGCTGAAGT	GTATTACAGC	CAAGTTATGA	CATCATCCGC	AAATGTTGTT	840
ATCATTTATG	GTGATACAGG	GAATACGTTA	GCTGTGAGCT	TTAGAATGTG	GGACTCTCTA	900
GGTATACAGA	GACTATGGGT	CACCACCTCA	CAGTGGGATG	TCACTCCTTT	TAAGAAAGAC	960
TTCACATTTG	ATAATGGATA	TGGAACTTTT	GGTTTTGGAC	ACCGCCACAG	TGAGATTTCT	1020
GGTTTTAAAT	ATTTTGTTCA	GACATTGAAC	CCTTTCAAAT	ACTCAGATGA	ATATTTGGTA	1080
		TAATTGTAAA				1140
AACTGCTCCT	TTAATCACTC	ATTGGAATGG	CTAATGACAC	ATACTTTTGA	CATGGCCATT	1200
ATTGAAGGGA	GTTATGAAAT	ATACAATGCT	GTGTATGCTT	TTGCCCATGC	ACTCCATGAG	1260
		TAATGTTCTC				1320
TGCAAGATGG	TTTATTCCTT	TCTGAGCAAG	ACTCAATTCA	CAAATCCTGT	TGGAGACACT	1380
GTGAATATGA	ATCAAAGAAA	CAAACTGAAG	GAAGAGTACG	ACATTTTCTA	CAATTGGAAT	1440
TTTCCACAGG	GACTTGGATT	TAAAGTGAAA	ATAGGAATAT	TTAGTCCATA	TTTTCCAAAA	1500
GGTCAACAGC	TTCATTTATC	TGAAAATCTG	ATAGAGTGGT	CCACAGGACG	TATACAGATG	1560
CCAACCTCTG	TGTGCAGTGC	CGATTGTGGT	CCTGGATTTA	GGAAAGTCTG	GAAGAATGGA	1620
ATGCCAGCCT	GTTGTTTTGA	CTGCAGTCCC	TGCCCAGAAA	ATGAAATTTC	TAATGAGACA	1680
AATGTGGAAT	TGTGTGTCCA	GTGTCCAGAG	GACCAATATG	CTAACCAAGA	GCAGAATCAC	1740
TGCATTCACA	AAGCTCGTAT	CTTTCTCTCT	TATGATGAAC	CCTTGGGGAT	GGCTCTTTCC	1800
	TATGCCTCGC			TTGGAGTCTT		1860
		GGCCAATAAC				1920
CTCATCTTTT	GTTTCCTCTG	CCCCTTGTTC	TTCATTGGCC	ATCCAAACTC	AGCTACCTGC	1980
ATCCTTCAGC	AAATCACATT	TGGAGTTGTG	TTCACTGTGG	CTATTTCCAC	TGTGTTGGCC	2040
AAAACAACCA	CTGTCATTCT	GGCTTTCAGA	GTCACAGCCC	CTCATAGAAT	GATGAAGTAC	2100
		TAACTACATC	ATTCCCATTT	GTACTCTCAT	TCAAATTATT	2160
GTATGTGCCA	TCTGGCTAGG	AGCTTCTCCT	CCTTCTGTTG	ATATTGATGC	ACAGTCTGAG	2220
	TCATCATTGC			CTGCTTTTTA		2280
		CTTTGTGAGC				2340
		CAAGTCCATG				2400
		TTACCATGGC				2460
		TAGTGCAGGA				2520
		AGACAGAAAT	TCTCTTCAAA	TGATCAGGGA	GAAGTCATCT	2580
TCTCATACTC	ACATTTTA					2598

(2) INFORMATION FOR SEQ ID NO:88:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2337 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

ATGAGGTTTG	CCATTGAGGA	AATCAACAGC	AATCCCCATC	TTTTACCAAA	CACATCCCTG	60
GGATTTGAGA	TCAATAATGT	CCCACACGGT	CAGAGGTACA	CTCTGGTCAA	ACTTTTTAGC	120
TCACTTTCAG	GGTCTAATTA	TGACATTCCT	AACTACATAA	GTGCAAGTGA	GAGCAATTCT	180
	TTACAGGACC	ATCGTGGACA	ATATCTGAAT	GCGTAGGGAC	ACTCCTGGAT	240
CTTTACAAAT	TTCCACAGCT	TACTTTTGGG	CCTTTTGATA	GTCTCCTGAG	TGAACAAAGA	300
CGGTTTTCTT	CTCTGTACCA	AGTGGCCCCC	AAAGATACAT	TTCTGACGCC	TGGCATTGTA	360
TCTTTGATGC	TTCATTTCCA	CTGGAACTGG	GTGGGGTTAT	TCATCATAGA	TGATGACAAA	420
GGTGCCCAGA	CACTGTCAGA	CTTGAGAAAT	GAGATGGATA	AAAATGGAGT	CTGCACAGCA	480
TTTGTAGAAA	TGATCCCAGT	CATCAAGGGT	TCATTTTTTA	CCAAATCCTG	GAAAAATCAT	540
GTGCAGATCC				ATGGGGACTC		600
TTAAGCTTAA	TAGTAAATAT	TAAGCAGAAG	TTGCTCACAT	GGAAAGTGTG	GGTACTGATC	660
	ATGTTTCTAA			TAGACTCATT		720
CTTATTTTTT	CACACCATCG	TGAGGAGATT	CCTAATTTTA	CAGATTTTAT	GCAGAAGTAC	780
AACCCTTCCA	AGTACCCGGA	AGACACTTAT	CTTCATGTAT	TGTGGCACAT	GTACTTCAAT	840
	TTAAGAAAGA			GTTTGCCTAA		900
GGGTTCTTGC	CTGGGAACAT	ATTTGACATG	GCCATGAGTG	AAGAGAGTTA	CAATGTATAC	960
AATGCTGTGT	ATGCTGTGGC	CCACAGTCTG	CATGAGATGA	TTCTCAACCA	AGTACAATTT	1020
CAAACTCATG	AAAAAGGAAA	AAAGATGGTA	TTCTTTCCTT	GGCAGCTTCA	CCCCTTTCTA	1080
AGGGAAAGAC	AACTCATCAA	TCAGAATGGA	GCGAATGAAG	ATCTGGATTG	TACCAGGAAG	1140
TCACATGTAG	AGTATGACAT	TCTCAACTTT	TGGAATTTCC	CAAAAGGTCT	TGGGCTAAAT	1200
	GAACGTTTTC					1260
	AGTGGGCCAC					1320
TGTCATCCTG	GATTCAGGAA	AACCCACCAG	GAAGGCAGGG	TTGCCTGTTG	CTTTGACTGC	1380
ATTCCTTGTC	CAGAAAATGA	GATCTCCAAT	GAGACAGATG	TGGATCAGTG	TGTGAAGTGT	1440
	ACTATGCAAA					1500
	ATGACCCATT					1560
CTCACAGCTG	CTGTTCTTGT	GGTGTTTCTG	AAGAACAGGG	ACACCCCCAT	TGTCAAGGCC	1620
	CTCTCAGTTA				TCTCTGTCCC	1680
TTGCTCTTCA	TTGGCCGTCC	CAGCACAGCC	TCCTGTATCC	TGCAGCAAAA	CATTTTTGGG	1740
CTTCTGTTCA	CTGTGGCTCT	TTCCACTGTG	TTGGCCAAAA	CTATCACTGT	GGTTATAGCC	1800
	CTTCTCCAGG			TGATATCAAG	GGCCCCTAAT	1860
	CCTTATGCAC			CTGGAATTTG	GCTGACAACC	1920
TCTCCTCCAT	TTATTGATAA	AGATGCTCAC	TCAGAACATG	GACACATCAT	CATCATTTGC	1980
	CAGCTGTTGC					2040
GTGAGCTACT	TTATGGCTTT	CTTGTCCAGA	AACCTACCTG	ACACATTCAA	TGAAGCCAAG	2100
	TCAGCATGCT				CCCTGTCTAC	2160
	AGGGGAAGAA				GGCTTCCAGT	2220
ACATCTCTCC	TAGGCATCAT	CTTTGCCCCC	AAGTGCTACC	TCATATTATT	AAGACCAGAA	2280
AGGAATTCAC	TTAGCTATAT	CAGGGACAAA	ACATATGCTA	AAAGCATAAA	ACCTTCT	2337

- (2) INFORMATION FOR SEQ ID NO:89:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1650 base pairs
 - (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

ATGCCTACGG	AAAACGATTA	TTTCAACCAG	ACTCTGAATA	TCCTAAAAAC	AACAAAAAAC	120
CACAAATATG	CTTTGGCATT	GGCCTTTTCA	ATTGATGAAA	TCAACAGGAA	TCCTGATCTT	180
TTACCAAATA	TGTCTTTGAT	CATAAAATAC	CCTTTGGGCC	TTTGCGATGG	ACAAACTACA	240
TTACCTACAC	CCTATTTATT	TAATGAAATA	TATTTTAGGC	CTATCCCTAA	TTATTTCTGT	300
AATGAAGAGA	CTATGTGTAC	ATTTCTACTT	ACAGGACCGC	ATTGGATAAC	ATCTTATAGT	360
TTCTGGATAC	ACTTGAACAT	CTTCTTATCT	CCTAGTATGA	ACCCAAAGGA	CACATCCCTA	420
GCTTTGGCAA	TGGTCTCCTT	CTTACTTTAT	TTCAAGTGGA	ACTGGGTCGG	CCTTGTCATC	480
TCAGATGATG	ATCAAGGCAA	TCAATTTCTC	TCTGAGTTGA	AAAAAGAGAG	CAAAATCAAG	540
GAAATTTGCT	TTGCATTTGT	GAGCATGCTG	GCAATCGATG	AGATTTCATT	TTATCATAAA	600
ACTGAAATGT		AATTGTGATG	TCATCCACAA	ACGTTATTAT	CATTTATGGG	660
	GTATTATTGA	GTTGAGCTTC	AGAATGTGGG	AATCTCCAGT	TATCCAGAGA	720
ATATGGGTCA		AATGAATTTC	CCTACCAGTA	AGAGAGATTT	AACTCATGAC	780
ACATTCTATG	GGACTCTTAC		AGCCATGGGG	AGATTTCAGG	CTTTAAAAAT	840
	CATGGTACCA	TCTTAGAATC	ACTGATTTGC	ATCTAGTAAT	GCCAGAGTGG	900
AAATATTTTA		CTCAGCATCT	AACTGTAAAA	TATTGAAGAA	CTATTCATCC	960
AGTGCCTCAT	TGGAATGGTT	AATGGAGCAG	ACATTTGACA	TGGTCTTTAG	TGATGGAAGT	1020
CGGGATATAT	ATAATGCTGT	AAATGCCATG	GCCCATGCAC	TCCATGAGAT	GAATCTGCAC	1080
CTGGTTGATA		AGACAATGGG	AAAGGAGCCA	GTTCTCACTG	CTTTAAGATA	1140
AACTCCTTTC	TCAGAAAGAC	CCACTTCACT	AATCCTCTTG	GGGACAGAGT	GATTATGAAA	1200
GAGAGAGAAA		AGACTATAAC		CTTGGAATTT	TTCTCAGCAC	1260
	AGGTGAAGAT	AGGAAAGTTC	AGCCCATATT	TTCCACATGG	CAGGCACTTT	1320
CACCTATATG	TAGACATGAT		ACAGGAAGTA	0.00.00.00	ATCCTCTGTG	1380
TGCACTGAAG	ATTGTAGTCC	TGGATACAGA	AGATTCTGGA	AGGAGGGAAT	GGCAGCCTGC	1440
TGTTTTGTTT	GCAGTCCCTG	CCCTGAAAAT	GCAATTTCTA	ATGAGACAAA	TATGGATCAG	1500
TGTGTGAATT	GTCCAGAATA	CCAATATGCC		GGGACAAATG	CATTCAGAAA	1560
AATGTGATGT			CTTGGGGATG	ACTCTTGCCT	TCATAGCCTT	1620
CTTTTTCTCT	GCATTAACAG	CTGTTGTACT				1650

(2) INFORMATION FOR SEQ ID NO:90:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2379 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

PTTCTCCT C	CAACATTCCA	CTTCTCATGG	CAAATTCCGT	TGATCCCAGG	60
ATAAATTT G	GAATGAAGTC	AAGGATATAG	ATTTAGATAC	AAGTTGTTAC	120
GCAGTTCA C	STTGCCTATG	GAGAAAGATT	ATTTCAACCA	GACTCTGAAT	180
	_				240
CCTCATAT 7					300
					360
					420
					480
					540
					600
					660
					720
					780
				CAGAACATGG	840
			AGTTGTATTT	CCCAACAAGT	900
				ACACCATGAT	960
		ACATGGTACC	ATCTCAAAAG	CATGGATTTA	1020
		GAATATGAAA	CCTCAGCATC	TTACTGTAAA	1080
AATTCATC G	SAATGTCTCA	TTGGAATGGC	TAATGGAACA	GAAGTTTGAC	1140
GACAATAG I	PCATAGTATA	TACAATGCTG	TGTACGCCAT	GGCCCATGCT	1200
AATCTGAA A	ACAAATTGAT	AATCAGGAAA	TCAGCTATGG	CAAAGGAGCA	1260
TTGAAGTT A	ACACTCATTT	TTGAGAACGA	TCCACTTCAC	CAATCCTTTT	1320
ATTATGAA A	AGAGAGAGTA	AGAGTGCAGG	AAGACTATGA	CATTGTTCAC	1380
					1440
GGACAATT 1	TATATTOAOT	GAAGACATGA	TTGATTTGGC	CACAGGAAGT	1500
	ATTANATTI GCAGTTCA ACCANATA CCTCATAT ANTATCCC ANTGANGA CTTTTCAT CATTCAT CATTCAT CATTCAT CATTCAT CATTCAT CATTCAT CATTCAT CATTCAT CACANCAC ATGANANA ATTTATGG ATCAGAG ATTANANA CCAGAGTG AATTCATC AATTCATCA ATTATGAA CCACAACA CCACAACA CCACAACA CCACAACA CCACAACA	ATTARATTT GAATGAAGTC GCAGTTCA GTTGCCTATG ACCAAATA CAACAGATAT TCTACCAAAC AATTACCC ACTCCGCTTA AATTACCA ACTCCGCTTA TCACTTGAAC TTTTCAT TCACTTGAAC TTTCAT TCACTTGAAC CATTACACA AGCATAGTCA ACATCACT AGCATTGCA ATTATAGA AACTGACATG ATTATAGG GGAACGACCC ATTACAGG GATATGGGT ACTCATGAAAT TTTTAAAA TTTTGTACAG CCAGAGTG GGTTTCTTT AATTCATC GAATGTCTCA AATCTGAA ACATTCATA TCTAAATTGAT ATTATGAA ACACTCATTT ATTATGAA ACACTCATTT ATTATGAA CCTTAGGATT	ATTANATTT GAATGAAGTC AAGGATATAG GCAGTTCA GTTGCCTATG GAGAAAGATT ACCAAATA CAACAGATAT GCATTGGCAT TTTACCAAAC ATGTCTTTGA AATGAAGA GACTATGTGT TCATTTATGC TTTTCAT TCACTTGAAC AATGAACAC ATGTCTTTTTCAT ACATCACT AGCATTGGCA ATGGTCTTT ACATCACT AGCATTGGCA ATGGTCTTT CTTGTCCT CTCAGATAAT GATGAACACC ATGAAAAA AACTGACATG TACTACAACC ATTATATGG GGAACGACCC AGTATTATTG ACATCACG GAAATATGC ATTAAAA TTTTGTACAG ACATGGTACC CCAGAGTG GGTTTCTTT CACTGAAAAA AACTGACATG AATTCATC GAATGCAACC AATTCATC GAATGCACC AATTCATC GAATGCACC AATTCATC GAATGCTC AATTCATC GAATGCTC AATTCATC ACACGCAAAACCA AATTCATC AAAATTGAAA ACACTCATTT ATGAAATGAAA ACACTCATTT ATGAAACAC ACACGCACACACACACACACACACACACACAC	ATTANATT GAATGAAGTC AAGGATATAG ATTTAGATAC GAGAGTCA GACCAAATA CAACCAGATAT GCATTGCAT TATTACCAACC ATTATACCA ACTCCACTTA TCACTTGACC ATTATCAT TCACTTGACC ATTATCAT TCACTTGACC ATTATCACT ACCACAC ACCACACAC ATTATCAT TCATTATAT TCACTTCAT TCACTTGACC ATTATCACT ACCACACAC AGAATATGC ATTATAGAA AACTGACAT ACCACACAC GAAATATGAT ACCACACAC GAATATCACAC AACATTCAT GAACACC AACATTCAT GAACACC AACATTCAT GAACACC ACCACACAC ACCACACAC ACCACACAC ACCACACAC ACCACACAC ACCACACAC ACCACACAC ACCACACAC ACCACACACAC ACCACACACACACACACACACACACACACACACACACACA	ATRANTT GANTGAAGTC ANGGATATAG ATTTAGATAC ANGTTGTTAC GAGTTCA GTTGCCTATG GAGANAGATT ATTTCAACCA GACTCTGAAT ACCANATA CAACAGATAT GCATTGGCAT TAGCCTTTAC ANTGGATGAA CCTCATAT TTTACCAAAC ATGTCTTTGA TTATAAAACA TACATTGGGC GAATTTTCCT TCAGTATT TCACTTGAAC ATCATTATCC TATTGGGAC GAATTTTCCT TCAGATTTCC TTATCAGTAT AATGAACAAT TCCTTATAT CTACACCAGATGAT AATGAACAAT TCCTTATAT CTACACCAGATGAT AATGAACAAT TCCTTATAT CTACACCGCA ACCACACAC GAAATTGGCA ATGGTCTCT TCATACTTTA CTACACGGA ATGAACACC GAAATTGTC TTTCAACTGG CACACACAC GGAAATATGC TTTGCCTTTG TGAACATGAT GCCAACACGA ACCACACAC AAATTGTGAA AACTGACAC AAATTGTGAT GCCAACACGA ACCACACGA ACCACACGA ACCACACAC ACCACACAC AACACCACACACA

AGAAAGATGC	CTTTATCTAT	GTGTAGTGCA	GATTGTCGTC	CTGGATACAG	AAAATTCTGG	1560
AAGGAGGAA	TGGCAGCCTG	CTGTTTTGTT	TGCAGTCCCT	GTCCAGACAA	TGAAATTTCT	1620
AATGAAACAA	CTGTGGTACT	TTGGGTCTTT	GTGAAGCACC	ATGACACTCC	TATTGTGAAG	1680
				TCATGTTCTG	CTTTCTGTGC	1740
		TCCTAACAGA		TCTTACAGCA	AATCACATTT	1800
		TGTTTCCACA		AAACAATCAC	TGTGCTTCTG	1860
		AGGAAGAAAG		TCCTGGTATC	GGGGACACCC	1920
		TTCCCTGTTG		TGTGTGCAAT	TTGGCTAGCA	1980
		TATCGATGAA		ATGGTCACAT	CATAATTGTG	2040
		GGCATTCTAC		GATATTTGGC	CTTCCTGGCC	2100
		TTTCTTGGCA		CTGACACATT	CAATGAAGCC	2160
		GCTAGTGTTC		GGATCACGTT	CCTTCCTGTC	2220
		AGTCATGGTT		TTTTCTCCAT	TTTGACATCC	2280
		CGTCTTTGCA		ACATCATTTT	AATGAAACCA	2340
GAGAGAATTC	TATCCAAAAG	ACAGGAGAAA	TCACGTTTC			2379

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2394 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

ATGGTAATAT TCTTCCTTCT CAACATTCCA TTTCTCCTGG CAAATTTCAT GGATCCCAGA TGCTTTTGGA AAATAAATTT GAATGAAATC AAGGATGAAG TCCTTGGGAT GACTTGTTCC 120 TTCATCCTTG AAACAGTTCA GAAGACTATG GACAAAGATT ATTTCAACCA GACTCTGAAT 180 GTCCTAAATA CAACTACAAA CCACAAATAT GCCTTGGCAT TGGCCTTTAC AGTGGATGAA ATCAACAGGA ATCCTGATCT TTTACCAAAT ATGTCTCTGA TTATAAAATA CAATTTGGGT 300 CATTGTGATG GAAAAACTGT AACAACTCTA TCCGATTTAT TTAATCCAAA TAATCATCTC CATTTCCCCA ATTATTTATG TAATGAAGGG ATTATGTGTT TGGTTCTGCT TACAGGACCA 420 CATTGGAGAG CATCTTTATA TCTCTGGATA TCCGTGTATG TCTACCTGTC TCCACATTTC
CTTCAGCTTT CCTATGGACC TTTCTACTCC ATCTTCAGTG ATAATGAACA ATATCCTTAT 540 CTCTATCAGA TGGGCCCAAA GGACTCATCA CTAGCATTGG CAATGGTCTC CTTCATAATT 600 TACTTCAAGT GGAACTGGGT TGGGCTATTT ATCTCAGATG ATGATCAAGG CAATCAATTT 660 CTCTCAGAGT TGAAAAAAGA GAGCCAAACC AAGGATATTT GCTTTGCCTT TGTGAACATG ATATCAGTCA GTGATGTTTC ATACTATCAT AAAACTGAAA TGTACTACAA CCAAATTGTG 780 ATGTCATCCA CAAAGGTTAT TATCATTTAT GGGGAAACAA ACAGTATTAT TGAATTGAGC 840 TTCAGAATGT GGTCATCTCC AGTTAAACAG AGAATATGGG TCACCACAAA ACAATTTGAT 900 TGCCCTACCA GTAAGAGAGA CTTAACTCAT GGCACATTCT ATGGGACCCT TACATTTCTA 960 CACCACTATG GTGAGATTTC TGGCTTTAAA AATTTTGTAC AGACACGGTA CAATCTCAGA 1020 AGCACAGATT TATATCTAGT AATGCCAGAG TGGAAATATT TTAACTATGA AGCCTCAGCA 1080 TCTAACTGTA AAATACTGAG AAACTATTTA TCCAATATCT CACTGGAATG GCTAATGGAA 1140 CAGAAATTTG ACATGTCATT TAGTGATTAT AGTCACAACA TATACAATGC TGTATATGCC ATTGCTCATG CACTCCATGA GAAGAATCTG CAAGAAGTTG AAAATCAGGC AATAAACAAT 1200 GCGAAAGGAG AAAATACTCA CTGCTTGAAG CTAAACTCAT TTCTGAGAAA GACCCACTTC 1320 ACTAATTCTC TTGGGAACAG AGTAATTATG AAACAGAGAG AAGTAGTGCA TGGAGACTAT AATATTGTTC ACATGTGGAA TTTCTCACAA CGCCTTGGGA TTAAGGTGAA GATAGGACAA 1440 TTCAGCCCAC ATTTTCCACA GGGTCAACAG TTACACTTAT ATGTAGACAT GACTGAGTTG GCTACAGGAA GTAGAAAGAT GCCATCCTCA GTGTGCAGTG CAGATTGCCA TCCTGGATTC AGAAGAATCT GGAAGGAGGA AATGGCAGCC TGCTGTTTTG TTTGCAACCC CTGCCTGAA 1560 1620 AATGAAATTT CTAATGAGAC GATGGTGGTA TTTTGGGTCT TCGTGAAGCA CCATGACACT 1680 CCTATTGTGA AGGCCAATAA CAGAATCCTC AGCTACCTAT TAATCGTGTC ACTCATGTTC 1740 TGTTTTCTGT GCTCCTTTTT CTTCATTGGC TATCCTAACA GAGCAACCTG TATCTTACAG CAAATCACAT TTGGAATCTT CTTTACTGTG GCTATTTCCA CAGTTCTGGC CAAAACAATC 1800 1860 ACTGTGGTTC TGGCTTTCAA AGTCACAGAC CCAGGAAGAC AATTAAGAAT CTTTTTGGTA 1920 TCGGGGACAC CCAACTACAT TATTCCCATA TGTTCCCTAT TGCAATGTAT TCTGTGTGCA 1980 ATCTGGCTAG CAGTTTCTCC TCCCTTTGTT GATATTGATG AACACTCTGA GCATGGCCAC 2040 ATCATCATTG TGTGCAACAA GGGCTCCATT ACTGCATTCT ACTGTGTCCT GGGATACTTG 2100 GCCTGCCTGG CCTTTGGAAG CTTCACTATA GCTTTCTTGG CAAAGAACCT GCCTGACACA 2160 TTCAACGAAG CCAAGTTCTT GACCTTCAGC ATGCTAGTGT TCTGCGCTGT CTGGGTCACC 2220

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TTCCTCCTG TCTACCATAG CACCAAGGGC AAGGTCATGG TTGCTGTGGA GATCTTCTCC 2280 ATCTTGGCAT CTAGTGCAGG GATGCTGGGA TGCATCTTTG CACCCAAAGT TTACATCATT
TTAATGAGAC CAGACAGAAA TTCGATCCAC AAAATCAGGG AGAAATCATA TTTC 2340 2394

(2) INFORMATION FOR SEQ ID NO:92:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2085 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

GTCTACCTGT	CTCCACATTT	CCTTCAGCTT	TCCTATGGAC	CTTTCTACTC	CATCTTCAGT	60
GATAATGAAC	AATATCCTTA	TCTCTATCAG	ATGGGCCCAA	AGGACTCATC	ACTAGCATTG	120
GCAATGGTCT	CCTTCATAAT	TTACTTCAAG	TGGAACTGGG	TTGGGCTATT	TATCTCAGAT	180
GATGATCAAG	GCAATCAATT	TCTCTCAGAG	TTGAAAAAAG	AGAGCCAAAC	CAAGGATATT	240
TGCTTTGCCT	TTGTGAACAT	GATATCAGTC	AGTGATGTTT	CATACTATCA	TAAAACTGAA	300
ATGTACTACA	ACCAAATTGT	GATGTCATCC	ACAAAGGTTA	TTATCATTTA	TGGGGAAACA	360
AACAGTATTA	TTGAATTGAG	CTTCAGAATG	TGGTCATCTC	CAGTTAAACA	GAGAATATGG	420
GTCACCACAA	AACAATTTGA	TTGCCCTACC	AGTAAGAGAG	ACTTAACTCA	TGGCACATTC	480
TATGGGACCC	TTACATTTCT	ACACCACTAT	GGTGAGATTT	CTGGCTTTAA	AAATTTTGTA	540
CAGACACGGT	ACAATCTCAG	AAGCACAGAT	TTATATCTAG	TAATGCCAGA	GTGGAAATAT	600
TTTAACTATG	AAGCCTCAGC	ATCTAACTGT	AAAATACTGA	GAAACTATTT	ATCCAATATC	660
TCACTGGAAT	GGCTAATGGA	ACAGAAATTT	GACATGTCAT	TTAGTGATTA	TAGTCACAAC	720
ATATACAATG	CTGTATATGC	CATTGCTCAT	GCACTCCATG	AGAAAGATCT	GCAAGAATTT	780
GAAAATCAGG	CAATAAACAA	TGCGAAAGGA	GAAAATACTC	ACTGCTTGAA	GCTAAACTCA	840
TTTCTGAGAA	AGACCCACTT	CACTAATTCT	CTTGGGAACA	GAGTAATTAT	GAAACAGAGA	900
GAAGTAGTGC	ATGGAGACTA	TAATATTGTT	CACATGTGGA	ATTTCTCACA	ACGCCTTGGG	960
ATTAAGGTGA	AGATAGGACA	ATTCAGCCCA	CATTTTCCAC	AGGGTCAACA	GTTACACTTA	1020
TATGTAGACA	TGACTGAGTT	GGCTACAGGA	AGTAGAAAGA	TGCCATCCTC	AGTGTGCAGT	1080
GCAGATTGCC	ATCCTGGATT	CAGAAGAATC	TGGAAGGAGG	AAATGGCAGC	CTGCTGTTTT	1140
GTTTGCAACC	CCTGCCCTGA	AAATGAAATT	TCTAATGAGA	CGAATATGGA	TCAGTGTGCG	1200
AATTGTCCAG	AATACCAGTA	TGCCAACACA	GAAAAGAACA	AATGCATCCA	GAAAGGTGTG	1260
ATTGTTCTAA	GCTATGAAGA	CCCCTTGGGG	ATGGCTCTTG	CCTTAATAGC	ATTCTGTTTC	1320
TCTGCATTCA	CAGTGGTGGT	ATTTTGGGTC	TTCGTGAAGC	ACCATGACAC	TCCTATTGTG	1380
AAGGCCAATA	ACAGAATCCT	CAGCTACCTA	TTAATCGTGT	CACTCATGTT	CTGTTTTCTG	1440
TGCTCCTTTT	TCTTCATTGG	CTATCCTAAC	AGAGCAACCT	GTATCTTACA	GCAAATCACA	1500
TTTGGAATCT	TCTTTACTGT	GGCTATTTCC	ACAGTTCTGG	CCAAAACAAT	CACTGTGGTT	1560
CTGGCTTTCA	AAGTCACAGA	CCCAGGAAGA	CAATTAAGAA	TCTTTTTGGT	ATCGGGGACA	1620
CCCAACTACA	TTATTCCCAT	ATGTTCCCTA	TTGCAATGTA	TTCTGTGTGC	AATCTGGCTA	1680
GCAGTTTCTC	CTCCCTTTGT	TGATATTGAT	GAACACTCTG	AGCATGGCCA	CATCATCATT	1740
GTGTGCAACA	AGGGCTCCAT	TACTGCATTC	TACTGTGTCC	TGGGATACTT	GGCCTGCCTG	1800
GCCTTTGGAA	GCTTCACTAT	AGCTTTCTTG	GCAAAGAACC	TGCCTGACAC	ATTCAACGAA	.1860
GCCAAGTTCT	TGACCTTCAG	CATGCTAGTG	TTCTGCGCTG	TCTGGGTCAC	CTTCCTCCCT	1920
GTCTACCATA	GCACCAAGGG	CAAGGTCATG	GTTGCTGTGG	AGATCTTCTC	CATCTTGGCA	1980
TCTAGTGCAG	GGATGCTGGG	ATGCATCTTT	GCACCCAAAG	TTTACATCAT	TTTAATGAGA	2040
CCAGACAGAA	ATTCGATCCA	CAAAATCAGG	GAGAAATCAT	ATTTC		2085

We claim:

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Claims

- 1. A family of pheromone receptor polypeptides, each of said polypeptides comprising from amino terminus to carboxyl terminus:
- 5 (a) an amino-terminal extracellular domain containing from 30 to 600 amino acids;
 - (b) a transmembrane region comprising:
 - (i) seven non-contiguous transmembrane domains designated TM1, TM2, TM3, TM4, TM5, TM6 and TM7
 - (ii) three non-contiguous extracellular domains designated EC2, EC3 and EC4, and
 - (iii) three non-contiguous intracellular domains designated IC1, IC2, and IC3,

wherein the transmembrane domains, the extracellular domains and the intracellular domains are attached to one another from amino terminus to carboxyl terminus in the order TM1-IC1-TM2-EC2-TM3-IC2-TM4-EC3-TM5-IC3-TM6-EC4-TM7, and

wherein the transmembrane region has at least about 35% homology and a length approximately equal to a transmembrane region of a polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50; and

- (c) a carboxyl-terminal intracellular domain containing from 5 to 200 amino acids; wherein the pheromone receptor polypeptides are expressed in a Gα_o protein-expressing vomeronasal organ neuron or are expressed in another olfactory organ neuron in an animal which does not possess a vomeronasal organ.
- 2. The polypeptides of claim 1, wherein the transmembrane region of each of said polypeptides has at least between about 60% and about 90% homology to the transdomain region of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50.
- 3. The polypeptides of claims 1 or 2, wherein the non-contiguous intracellular domains of each of said polypeptides has at least between about 60% and about 90% homology to the non-contiguous intracellular domains of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 34, 36, 38, 40, 42, 44, 46, 48, and 50.

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4. The polypeptides of claim 1, wherein the extracellular domain of each of said polypeptides has at least between about 50% and about 90% homology to the extracellular domain of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, and 50.

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5. The polypeptides of claim 2, wherein the extracellular domain of each of said polypeptides has at least between about 50% and about 90% homology to the extracellular domain of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, and 50.

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6. The polypeptides of claim 3, wherein the extracellular domain of each of said polypeptides has at least between about 50% and about 90% homology to the extracellular domain of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, and 50.

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- 7. The polypeptides of claims 1 or 2, wherein the extracellular domain contains at least between about 50 and about 500 amino acids.
- 8. The polypeptides of claim 3, wherein the extracellular domain contains at least between about 50 and about 500 amino acids.
 - 9. The polypeptides of claims 4, 5 or 6, further comprising a signal sequence attached to the amino terminus of the extracellular domain.
- 10. The polypeptides of claim 9, wherein the signal sequence is selected from the group of signal sequences of a pheromone receptor polypeptide of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
- 11. A method for identifying a nucleic acid encoding a pheromone receptor polypeptide, 0 comprising:
 - (1) contacting a mixture of nucleic acid molecules with at least one nucleic acid probe of a nucleic acid selected from the group consisting of: (a) a nucleic acid molecule selected from

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the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55 that encodes a pheromone receptor polypeptide; (b) a unique fragment of (a); (c) a human homolog of (a) or (b); and (d) a set of degenerate primers of any of (a), (b) or (c); and

- (2) identifying the sequences within the mixture that hybridize to the probe.
- 12. The method of claim 11, wherein the mixture is a genomic library.
- 13. The method of claim 11, wherein the mixture is a cDNA library.

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- 14. The method of claim 11, wherein the nucleic acid probe contains a detectable label.
- 15. The method of claim 11, wherein the at least one nucleic acid probe is a pair of degenerate polymerase chain reaction primers that amplify a unique fragment of a nucleic acid molecule selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55, the method further comprising the step of subjecting the mixture to a polymerase chain reaction amplification reaction prior to selecting a member of the mixture which hybridizes to the nucleic acid probe.
- 16. The method of claim 15, wherein the pair of degenerate polymerase chain reaction primers is selected from the group consisting of SEQ ID NOs. 60 and 61, SEQ ID NOs. 62 and 63, SEQ ID NOs. 64 and 63, SEQ ID NOs. 64 and 65, and SEQ ID NOs. 66 and 67.
- 17. The method of claim 16, wherein the pair of polymerase chain reaction primers is selected from the group consisting of SEQ ID NOs. 60 and 61, SEQ ID NOs. 62 and 63, SEQ ID and NOs. 64 and 63.

18. An isolated nucleic acid molecule

(a) which hybridizes under high or low stringency conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, and 55, and which codes for a pheromone receptor,

- (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and
 - (c) complements of (a) and (b).

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- 5 19. The nucleic acid molecule of claim 18, wherein the pheromone receptor is expressed in the vomeronasal organ or is expressed in another olfactory organ in an animal which does not possess a vomeronasal organ.
- 20. The nucleic acid molecule of claim 18, wherein the pheromone receptor is expressed in a $G\alpha_0$ protein-expressing vomeronasal organ neuron.
 - 21. The nucleic acid molecule of claim 18, wherein the pheromone receptor is a G-protein coupled receptor.
- 15 22. The isolated nucleic acid molecule of claim 18, wherein the pheromone receptor has an amino acid sequence selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
 - 23. The isolated nucleic acid molecule of claim 18, wherein the isolated nucleic acid molecule is selected from the group consisting of SEQ ID NO. 51, 53, 54, 55, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, and 92, that encodes a pheromone receptor polypeptide.
- 24. The isolated nucleic acid molecule of claim 18, wherein the isolated molecule comprises a molecule having a sequence which encodes a pheromone receptor unique fragment, wherein said unique fragment is selected from the group consisting of a pheromone receptor extracellular domain, a pheromone receptor transmembrane domain, a pheromone receptor extracellular domain, a pheromone receptor extracellular domain coupled to at least one transmembrane domain, and at least one pheromone receptor transmembrane domain coupled to a pheromone receptor intracellular domain.

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- 25. The isolated nucleic acid molecule of claim 18, wherein the pheromone receptor extracellular domain, the pheromone receptor transmembrane domain and the pheromone receptor intracellular domain have amino acid sequences selected from the group of sequences identified as these domains in SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
- 26. The isolated nucleic acid molecule of claim 18, wherein the unique fragment is selected from the group consisting of between 12 and 4000, between 12 and 2000, between 12 and 1000, between 12 and 500, between 12 and 250, between 12 and 100, between 12 and 50, and between 12 and 25, nucleotides in length.
- 27. An isolated nucleic acid molecule, comprising
- (a) a molecule having a sequence selected from the group consisting of SEQ ID NO. 51, 53, 54, 55, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, and 92, and which codes for a pheromone receptor;
- (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and
 - (c) complements of (a) and (b).
- 28. An expression vector comprising the isolated nucleic acid molecule of claims 18-27 operably linked to a promoter.
 - 29. A host cell transformed or transfected with the isolated nucleic acid molecule of claims 18-27.
 - 30. A host cell transformed or transfected with the isolated nucleic acid molecule of the expression vector of claim 28.
- An isolated polypeptide encoded by the isolated nucleic acid molecule of claims 18-27.
 - 32. The isolated polypeptide of claim 31, wherein the isolated polypeptide has a pheromone receptor activity.

- 33. The isolated polypeptide of claim 31, wherein the isolated polypeptide comprises a polypeptide selected from group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
- The isolated polypeptide of claim 33, wherein the isolated polypeptide is a fragment of a peptide selected from the group consisting of an extracellular domain, a transmembrane domain and an intracellular domain, wherein the foregoing domains have amino acid sequences selected from the group of sequences identified as these domains of a pheromone receptor polypeptide selected from group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
 - 35. A vaccine containing an isolated polypeptide selected from the group consisting of the isolated polypeptides of claim 31, 32, 33, and 34.
- 15 36. A method for controlling fertility in an animal, comprising:

 administering to an animal in need of such treatment, an effective amount of the vaccine of claim 35 to elicit an immune response to the isolated polypeptide.
- An isolated binding polypeptide which binds selectively to a polypeptide of claim 1, 2,
 4, 5, 6, 8, 10, 31, 32, 33, and 34, provided that the isolated binding polypeptide does not bind to a G-protein coupled receptor other than a Gα₀⁺-coupled pheromone receptor.
- 38. The isolated binding polypeptide of claim 37, wherein the binding polypeptide binds to a polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50 and 52.
- 39. The isolated binding polypeptide of claim 37, wherein the binding polypeptide is an antibody fragment selected from the group consisting of a Fab fragment, a F(ab)₂ fragment or a fragment including a CDR3 region selective for a pheromone receptor polypeptide.

40. The isolated binding polypeptide of claim 38, wherein the binding polypeptide is an antibody fragment selected from the group consisting of a Fab fragment, a F(ab)₂ fragment or a fragment including a CDR3 region selective for a pheromone receptor polypeptide.

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41. An affinity matrix comprising:

a solid support to which is coupled an isolated binding polypeptide selected from the group consisting of the binding polypeptides of any of claims 37740.

10 42. A method for isolating a pheromone receptor, comprising:

contacting a composition containing a putative pheromone receptor with the affinity matrix of claim 41 under conditions to permit the pheromone receptor to selectively bind to the binding polypeptides coupled to the solid support; and

isolating the polypeptides that bind to the affinity matrix.

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43. A composition comprising:

the polypeptide of claim 1, 2, 4, 5, 6, 8, 10, 31, 32, 33, or 34; and a pharmaceutically acceptable carrier.

20 44. A composition comprising:

the nucleic acid molecule of any of claims 18-28; and a pharmaceutically acceptable carrier.

- 45. A composition comprising:
- 25 the binding polypeptide of claim 37; and a pharmaceutically acceptable carrier.
 - 46. A composition comprising:

the binding polypeptide of claims 38, 39 or 40; and

- a pharmaceutically acceptable carrier.
 - 47. A method for modulating a pheromone receptor activity in a cell, comprising;

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administering to the cell an amount of the isolated binding polypeptide of claim 37 effective to modulate pheromone receptor activity in the cell.

- 48. A method for modulating a pheromone receptor activity in a cell, comprising:

 administering to the cell an amount of the isolated binding polypeptide of claim

 38, 39, or 40 effective to modulate pheromone receptor activity in the cell.
 - 49. The method of claim 47, wherein modulating a pheromone receptor activity comprises reducing the pheromone receptor activity.
- 50. The method of claim 48, wherein modulating a pheromone receptor activity comprises reducing the pheromone receptor activity.
- 51. The method of claim 47, wherein the pheromone receptor activity is selected from the group consisting of a signal transduction activity and a ligand binding activity.
 - 52. The method of claim 48, wherein the pheromone receptor activity is selected from the group consisting of a signal transduction activity and a ligand binding activity.
- The method of claim 47, wherein the cell is a vertebrate cell, preferably a mammalian cell.
 - 54. The method of claim 48, wherein the cell is a vertebrate cell, preferably a mammalian cell.
 - 55. The method of claim 47, wherein the cell is an invertebrate cell, preferably an insect cell.
 - 56. The method of claim 48, wherein the cell is an invertebrate cell, preferably an insect cell.
- 30 57. A method for reducing the binding of a pheromone having a binding domain to a pheromone receptor having a ligand binding site that selectively binds to the binding domain of the pheromone, comprising:

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contacting the pheromone receptor with an agent which binds to the binding domain for a time effective to reduce binding of the pheromone to the ligand binding site of the pheromone receptor.

- 5 58. The method of claim 57, wherein the agent is an antibody which binds to the binding domain.
 - 59. A method for decreasing pheromone receptor mediated signal transduction activity in a subject comprising:
- administering to a subject in need of such treatment an agent that selectively binds to an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount effective to decrease pheromone receptor mediated signal transduction activity in the subject.
- 15 60. The method of claim 59, wherein the agent is selected from the group consisting of an antisense nucleic acid and a binding polypeptide.
 - 61. A method for identifying lead compounds for a pharmacological agent useful in the diagnosis or treatment of disease associated with pheromone binding to a pheromone receptor polypeptide containing a ligand binding site that selectively binds to a binding domain of the pheromone, comprising

forming a mixture comprising a pheromone receptor polypeptide or unique fragment thereof containing a ligand binding site, a molecule protein containing a binding domain which selectively binds the pheromone receptor ligand binding site, and a candidate pharmacological agent,

incubating the mixture under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of selective binding of the molecule containing a ligand binding domain by the pheromone receptor ligand binding site, and

detecting a test amount of selective binding of the molecule containing the binding domain by the pheromone receptor ligand binding site, wherein reduction of the test amount of selective binding relative to the first amount of selective binding indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which disrupts selective

binding of a molecule containing a binding domain by a pheromone receptor containing a ligand binding site and wherein increase of the test amount of selective binding relative to the first amount of selective binding indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which enhances selective binding of a molecule containing a binding domain by a pheromone receptor polypeptide containing a ligand binding site.

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AMENDED CLAIMS

[received by the International Bureau on 11 December 1998 (11.12.98); original claim 1 amended; remaining claims unchanged (1 page)]

- 1. A family of isolated pheromone receptor polypeptides, each of said isolated polypeptides comprising from amino terminus to carboxyl terminus:
- 5 (a) an amino-terminal extracellular domain containing from 30 to 600 amino acids;
 - (b) a transmembrane region comprising:
 - (i) seven non-contiguous transmembrane domains designated TM1, TM2, TM3, TM4, TM5, TM6 and TM7
 - (ii) three non-contiguous extracellular domains designated EC2, EC3 and EC4, and
 - (iii) three non-contiguous intracellular domains designated IC1, IC2, and IC3, wherein the transmembrane domains, the extracellular domains and the intracellular domains are attached to one another from amino terminus to carboxyl terminus in the order TM1-IC1-TM2-EC2-TM3- IC2-TM4-EC3-TM5-IC3-TM6-EC4-TM7, and

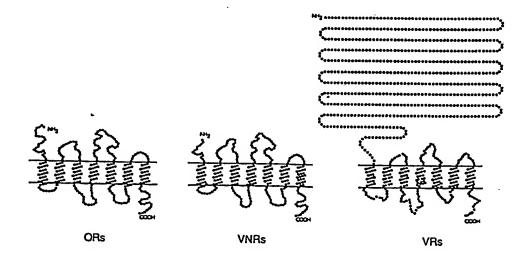
wherein the transmembrane region has at least about 35% homology and a length approximately equal to a transmembrane region of a polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50; and

- (c) a carboxyl-terminal intracellular domain containing from 5 to 200 amino acids; wherein the pheromone receptor polypeptides are expressed in a Gα_o proteinexpressing vomeronasal organ neuron or are expressed in another olfactory organ neuron in an animal which does not possess a vomeronasal organ.
- 2. The polypeptides of claim 1, wherein the transmembrane region of each of said polypeptides has at least between about 60% and about 90% homology to the transdomain region of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 34, 36, 38, 40, 42, 44, 46, 48, and 50.
- 3. The polypeptides of claims 1 or 2, wherein the non-contiguous intracellular domains of each of said polypeptides has at least between about 60% and about 90% homology to the non-contiguous intracellular domains of a pheromone receptor polypeptide selected from the group consisting of SEQ ID NO. 2, 4, 6, 8, 10, 34, 36, 38, 40, 42, 44, 46, 48, and 50.

FIBURE 1.

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FIBURE 2.



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FIGURE 3.

International application No. PCT/US98/13680

	101/0398/13080				
A. CLASSIFICATION OF SUBJECT MATTER IPC(6) :C07K 14/705; C12N 15/12; A61K 38/17; C12Q 1/68 US CL :536/23.5, 24.31; 530/350; 514/2; 435/6 According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED					
Minimum documentation searched (classification system follo	wed by classification symbols)				
U.S. : 536/23.5, 24.31; 530/350; 514/2; 435/6					
Documentation searched other than minimum documentation to	the extent that such documents are included in th	e fields searched			
Electronic data base consulted during the international search	(name of data base and where provided and	-h			
APS, Biosis, Medline, WPI search terms: pheromone receptor, odorant receptor, vomero		ch terms used)			
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category* Citation of document, with indication, where	appropriate, of the relevant passages Re	elevant to claim No.			
BROWN et al. Cloning and Characterization of an Extracellular Ca ²⁺ -Sensing Receptor from Bovine Parathyroid. Nature. 09					
Y December 1993, Vol. 366, pages 575-580, pages 577 and 578. 1-17, 22, 23, 27, 43					
KIEFER et al. Expression of an Olicoli: Purification, Reconstitution Biochemistry. 1996, Vol. 35, No. 3	tion, and Ligand Binding. 50, pages 16077-16084.	27, 43			
X Further documents are listed in the continuation of Box	C. See patent family annex.				
Special categories of cited documents: A* document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the internationa date and not in conflict with the application be the principle or theory underlying the invention	ut cited to understand			
B* earlier document published on or after the international filing date	"X" document of particular relevance; the claimed	invention cannot be			
L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	when the document is taken alone	olve an inventive step			
O* document referring to an oral disclosure, use, exhibition or other means	"Y" document of particular relevance; the claimed considered to involve an inventive step with combined with one or more other such docume being obvious to a person skilled in the art	hen the document is I			
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International application No.
PCT/US98/13680

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT Category* Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X, P HERRADA et al. A Novel Family of Putative Pheromone 1-27, 43 (Species Receptors in Mammals with a Topographically Organized and Sexually Dimorphic Distribution. Cell. 22 August 1997, Vol. 90, pages 763-773, see pages 765-767. X, P MATSUNAMI et al. A Multigene Family Encoding a Diverse 1-27, 43 Array of Putative Pheromone Receptors in Mammals. Cell. 22 (species 1 and 4) August 1997, Vol. 90, pages 775-784, pages 776-778.

Form PCT/ISA/210 (continuation of second sheet)(July 1992)*

International application No. PCT/US98/13680

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)					
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:					
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:					
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:					
3. X Claims Nos.: 28-42, 44-56 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).					
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)					
This International Searching Authority found multiple inventions in this international application, as follows:					
Please See Extra Sheet.					
I. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.					
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.					
As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-27 and 43, species 1, 4, 17, 26-29					
No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:					
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.					

International application No. PCT/US98/13680

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-27, 43, drawn to pherome receptor polypeptides and their encoding nucleic acids.

Group II, claims 57 and 58, drawn to a method of reducing the binding of a pheromone to a pherome receptor.

Group III, claims 59 and 60, drawn to a method of decreasing pherome receptor mediated signal transduction.

Group IV, claim 61, drawn to a method of identifying lead compounds.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

```
1) SEQ ID NO: 1 and 2;
 2) SEQ ID NO: 3 and 4;
 3) SEQ ID NO: 5 and 6;
 4) SEQ ID NO: 7 and 8;
 5) SEQ ID NO: 9 and 10;
 6) SEQ ID NO: 11 and 12;
 7) SEQ ID NO: 13 and 14:
 8) SEQ ID NO: 15 and 16;
 9) SEQ ID NO: 17 and 18;
 10) SEQ ID NO: 19 and 20;
 11) SEQ ID NO: 21 and 22;
 12) SEQ ID NO: 23 and 24;
 13) SEQ ID NO: 25 and 26;
 14) SEQ ID NO: 27 and 28;
 15) SEQ ID NO: 29 and 30;
 16) SEQ ID NO: 31 and 32;
17 SEQ ID NO: 33 and 34;
 18 SEQ ID NO: 35 and 36;
19) SEQ ID NO: 37 and 38;
20) SEQ ID NO: 39 and 40;
21) SEQ ID NO: 41 and 42;
22) SEQ ID NO: 43 and 44;
23) SEQ ID NO: 45 and 46;
24) SEQ ID NO: 47 and 48:
25) SEQ ID NO: 49 and 50;
26) SEQ-ID NO: 51 and 52;
27) SEQ ID NO: 53;
28) SEQ ID NO: 54;
29) SEQ ID NO: 55;
30) SEQ ID NO: 68:
31) SEQ ID NO: 69;
32) SEQ ID NO: 70:
33) SEQ ID NO: 71;
34) SEQ ID NO: 72;
35) SEQ ID NO: 73;
36) SEQ ID NO: 74;
37) SEQ ID NO: 75;
38) SEQ ID NO: 76;
39) SEQ ID NO: 77;
40) SEQ ID NO: 78;
41) SEQ ID NO: 79;
42) SEQ ID NO: 80;
43) SEQ ID NO: 81:
44) SEQ ID NO: 82;
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45) SEQ ID NO: 83;

International application No. PCT/US98/13680

46) SEQ ID NO: 84; 47) SEQ ID NO: 85; 48) SEQ ID NO: 86; 49) SEQ ID NO: 87; 50) SEQ ID NO: 88; 51) SEQ ID NO: 89; 52) SEQ ID NO: 90; 53) SEQ ID NO: 91; 54) SEQ ID NO: 92.

The claims are deemed to correspond to the species listed above in the following manner:

The claims are directed to pheromone receptor polypeptides and their encoding nucleic acids having the recited sequences.

The following claims are generic: 1-27, 43, and 57-61.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: It is noted that the expression "special technical features" is defined in Rule 13.2 as meaning "those technical features that define a contribution which each of the inventions, considered as a whole makes over the prior art". The claimed invention of Group I, directed to a family of pheromone receptor polypeptide, encompasses naturally occurring non-isolated products present in the vomeronasal organ and is anticipated by the prior art (see Dulac and Axel). Therefore, the polypeptide of Group I lacks a special technical feature. The special technical feature of Group II is a method of using a binding protein to reduce the binding of the pheromone receptor to its ligand. The special technical feature of Group III is a method of using a compound that binds to the nucleic acid encoding a pheromone receptor to decrease pheromone receptor mediated signal transduction. The special technical feature of Group IV is a method of identifying lead compounds for a pharmacological agent useful in the diagnosis or treatment of disease associated with pheromone binding to a pheromone receptor. The special technical feature of each group is not the same or does not correspond to the special technical feature of any other group because the methods of Groups II, III, and IV require different starting reagents and method steps to accomplish different goals. The Groups are not linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the species has a distinct amino acid sequence and is encoded by a distinct nucleic acid sequence.

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International application No.
PCT/US98/13680

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2Xa) for the following reasons:
1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
·
2. Claims Nos.:
because they relate to parts of the international application that do not consider the
an extent that no meaningful international search can be carried out, specifically:
3. X Claims Nos.: 28-42, 44-56
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet
·
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid specifically elements.
only those claims for which fees were paid, specifically claims Nos.: 1-27 and 43, species 1, 4, 17, 26-29
1, 4, 17, 20-29
*
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.